

# BMJ Open Heart failure in patients presenting with dyspnoea to the emergency department in the Asia Pacific region: an observational study

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## ABSTRACT

**Objectives:** To describe demographic features, assessment, management and outcomes of patients who were diagnosed with heart failure after presenting to an emergency department (ED) with a principal symptom of dyspnoea.

**Design:** Planned substudy of the prospective, descriptive cohort study: Asia, Australia and New Zealand Dyspnoea in Emergency Departments (AANZDEM).

**Setting:** 46 EDs in Australia, New Zealand, Singapore, Hong Kong and Malaysia collected data over 3 72-hour periods in May, August and October 2014.

**Participants:** Patients with an ED diagnosis of heart failure.

**Outcome measures:** Outcomes included patient epidemiology, investigations ordered, treatment modalities used and patient outcomes (hospital length of stay (LOS) and mortality).

**Results:** 455 (14.9%) of the 3044 patients had an ED diagnosis of heart failure. Median age was 79 years, half were male and 62% arrived via ambulance. 392 (86%) patients were admitted to hospital. ED diagnosis was concordant with hospital discharge diagnosis in 81% of cases. Median hospital LOS was 6 days (IQR 4–9) and in-hospital mortality was 5.1%. Natriuretic peptide levels were ordered in 19%, with lung ultrasound (<1%) and echocardiography (2%) uncommonly performed. Treatment modalities included non-invasive ventilation (12%), diuretics (73%), nitrates (25%), antibiotics (16%), inhaled  $\beta$ -agonists (13%) and corticosteroids (6%).

**Conclusions:** In the Asia Pacific region, heart failure is a common diagnosis among patients presenting to the ED with a principal symptom of dyspnoea. Admission rates were high and ED diagnostic accuracy was good. Despite the seemingly suboptimal adherence to investigation and treatment guidelines, patient outcomes were favourable compared with other registries.

## INTRODUCTION

Shortness of breath is a common and frightening symptom, which often leads patients

## Strengths and limitations of this study

- This is one of the first studies to collect data on patients with heart failure in the Asia Pacific.
- Data were prospectively collected on consecutive patients with a predefined data dictionary and using an online database.
- Dyspnoea as inclusion criteria is novel and patient-centred, but may limit comparison with other heart failure registries.
- The diagnosis of heart failure was based on clinician judgement, with limited echo performed in emergency department, reflecting real-world practice.

to present to emergency departments (EDs).<sup>1</sup> The recent EuroDEM pilot study found that 22% of patients had a cardiac cause for their dyspnoea, with heart failure (HF) as the most common diagnosis (personal communication, Laribi, EuroDEM pilot study, MEMC Congress, Marseilles, France, September 2013). Approximately 1–2% of the adult population in developed countries has HF, with the prevalence rising to  $\geq 10\%$  among patients over the age of 70.<sup>2</sup> The symptoms of HF progressively deteriorate over time, and as such it has an important impact on quality of life. Acute decompensation often leads to hospital admission.

The AANZDEM study,<sup>3 4</sup> built on the methodology of the EuroDEM study (as shared by Laribi), aimed to establish how common shortness of breath was as a symptom in the ED patient population and to describe epidemiological features of patients, distribution of investigations and treatments as well as diagnosis and clinical outcomes. This substudy provides a new insight into ED patients with HF, based on their presenting symptom of breathlessness.

Several HF registries exist and a recent summary paper<sup>2</sup> highlighted major regional differences in the severity, aetiology, management and outcomes of patients with HF in clinical trials and registries. A paucity of data collected outside North America and Europe was noted with a call for further data about geographical variation outside these regions.

To address these unanswered questions, Ambrosy *et al*<sup>2</sup> suggested that a (hospital-based) registry is required which is geographically representative and employs consecutive or intermittently consecutive enrolment and captures comprehensive and longitudinal data including hospital course and postdischarge outcomes.

Moreover, leading international organisations have developed guidelines for the assessment and management of patients with acute HF.<sup>5 6</sup> Adherence to these evidence-based guidelines is important but often difficult to measure due to lack of accurate data. This study will also be able to provide insight in adherence to existing guidelines.

We aim to describe a cohort of patients attending an ED in the Asia Pacific region with a principal symptom of dyspnoea and an ED diagnosis of HF in terms of demographics, clinical characteristics, investigations ordered, treatments and patient outcomes (final diagnosis, hospital length of stay (LOS) and in-hospital mortality).

## METHODS

This is a planned substudy of the AANZDEM study. The methodology of that study, including definitions of clinical variables, has been published previously.<sup>3 4</sup> In summary, it was a prospective, descriptive cohort study conducted in EDs in Australia, New Zealand, Singapore, Hong Kong and Malaysia of consecutive adult patients presenting to the ED with dyspnoea as a main symptom (eg, includes patients who had chest pain as well as dyspnoea). Data were collected over three 72-hour periods in May, August and October 2014 (autumn, winter and spring in Australasia) and included demographics, comorbidities, mode of arrival, usual medications, pre-hospital treatment, initial assessment, ED investigations, treatment in the ED, ED diagnosis, disposition from ED, in-hospital outcome and final hospital diagnosis. Participating hospitals also provided data on total ED presentations and admissions (ward or intensive care unit (ICU)) for each data collection window.

This substudy includes the patients in the AANZDEM study with an ED diagnosis of HF. Patients were included if the principle diagnoses entered by the treating clinician in the ED information system or in the (electronic) medical records included HF, decompensated HF, right-sided HF or acute pulmonary oedema. The primary outcomes of interest are the epidemiology, investigations ordered, treatments given and overall outcomes of these patients. Secondary outcomes were geographical variation.

Analysis was by descriptive statistics, comparisons of proportions and measures of associations ( $\chi^2$ /Fisher's

exact test). Non-parametric data were compared using the Mann-Whitney U test. Analysis programs included Analyse-It,<sup>7</sup> Statistical Package for the Social Sciences (V.22) and Vassar stats.<sup>8</sup> For analysis by region, Australia and New Zealand data were combined due to the small number of New Zealand patients (N=28) and compared against the nine South East Asian EDs. A formal sample size calculation was not performed, as this is a descriptive study. Reporting complies with the STROBE guidelines.<sup>9</sup>

Human research ethics approvals for the overall study, as well as predefined substudies, were obtained for all sites according to local requirements. In most jurisdictions, patient consent for data collection was not required.

## RESULTS

Forty-six EDs contributed data on 3044 patients. Thirty-three sites were located in Australia, four in New Zealand, four in Hong Kong, three in Singapore and two in Malaysia. In 2014, the study sites had a combined annual ED census of 2 886 178 patients.

### Demographics and comorbidities

Four hundred and fifty-five patients (14.9%) had an ED diagnosis of HF. This represents 0.76% (95% CI 0.69% to 0.83%) of all ED attendances in the study periods.

Patient characteristics (overall and by geographical region) are described in [table 1](#). The overall median age was 79 years (IQR 67–87), half were male and 62% arrived via ambulance. Patients in South East Asia were younger (median age 73 vs 81 years,  $p<0.001$ ) and less likely to present by ambulance (52% vs 67%,  $p=0.002$ ). Common comorbidities included hypertension (72%), previous diagnosis of HF (57%), ischaemic heart disease (53%), hyperlipidaemia (47%), diabetes (43%) and previous atrial fibrillation (AF; 40%).

Patients in South East Asia were significantly less likely to have a history of HF (44% vs 57%,  $p=0.003$ ), previous AF (30% vs 40%,  $p=0.004$ ), valvular disease ( $p<0.001$ ), chronic obstructive pulmonary disease (COPD;  $p<0.001$ ) or active malignancy ( $p=0.004$ ) as comorbidities.

### Medications

Common regular medications patients were prescribed before presentation are also described in [table 1](#) and included: diuretics (62%), statins (52%), antiplatelet agents (50%),  $\beta$ -blockers (49%) and ACE inhibitors or aldosterone receptor antagonists (ACEi/angiotensin receptor blocker (ARB); 48%). Patients from the South East Asian countries had a significantly lower use of diuretics (54%) and ACEi/ARB (39%), in line with the lower proportion of patients with a history of HF in these countries.

### Clinical features

Examination findings are shown in [table 2](#). Overall, on presentation to ED, 53% of patients had a systolic blood pressure over 140 mm Hg and three-quarters of the

**Table 1** Patient characteristics: overall, by region and by season

	Overall	By region		p Value
	Overall (N=455)	Australia and NZ (N=312)	SE Asia (N=143)	
<b>Demographics</b>				
Age (years, median, IQR)	79 (67–87)	81 (69–88)	73 (63–82)	<0.001
Gender (N, % male, 95% CI)	227; 50% (45% to 55%) Missing data=1	149; 48% (43% to 53%) Missing data=0	78; 55% (47% to 63%) Missing data=1	0.12
Ambulance arrival (N, %, 95% CI)	280; 62% (58% to 67%) Missing data=6	67% (62% to 73%) Missing data=6	52% (44% to 60%) Missing data=0	0.002
<b>Comorbidities</b>				
<i>N, % (95% CI)</i>				
Hypertension	327; 72% (68% to 76%) Missing data=1	221; 71% (66% to 76%) Missing data=1	106; 74% (66% to 81%) Missing data=0	0.50
Previous heart failure	256; 57% (52% to 61%) Missing data=2	193; 62% (57% to 67%) Missing data=2	63; 44% (36% to 52%) Missing data=0	0.0003
IHD	239; 53% (48% to 57%) Missing data=1	161; 52% (46% to 57%) Missing data=1	78; 55% (46% to 62%) Missing data=0	0.58
Dyslipidaemia	212; 47% (42% to 52%) Missing data=4	147; 48% (42% to 53%) Missing data=4	65; 45% (38% to 54%) Missing data=0	0.65
Diabetes	194; 43% (39% to 48%) Missing data=4	131; 43% (37% to 48%) Missing data=4	63; 44% (36% to 52%) Missing data=0	0.76
Prior AF	180; 40% (35% to 44%) Missing data=3	137; 44% (39% to 50%) Missing data=3	43; 30% (23% to 38%) Missing data=0	0.004
Renal impairment	127; 28% (24% to 33%) Missing data=5	86; 28% (23% to 33%) Missing data=5	41; 29% (22% to 37%) Missing data=0	0.88
COPD	83; 18% (15% to 22%) Missing data=5	77; 25% (21% to 30%) Missing data=5	6; 4% (2% to 9%) Missing data=0	<0.0001
Valvular disease	69; 15% (12% to 18%) Missing data=5	61; 20% (16% to 25%) Missing data=5	6; 4% (2% to 9%) Missing data=0	<0.0001
Anaemia	57; 13% (10% to 16%) Missing data=5	34; 11% (8% to 15%) Missing data=5	23; 16% (11% to 23%) Missing data=0	0.13
Smoker	35; 8% (6% to 11%) Missing data=5	27; 9% (6% to 12%) Missing data=5	8; 6% (3% to 11%) Missing data=0	0.23
Active malignancy	37; 8% (6% to 11%) Missing data=4	33; 11% (8% to 15%) Missing data=4	4; 3% (1% to 7%) Missing data=0	0.004
Prior PE	17; 4% (2% to 6%) Missing data=5	15; 5% (3% to 8%) Missing data=5	2; 1% (0.4% to 5%) Missing data=0	0.07
<b>Usual medications</b>				
<i>N, % (95% CI)</i>				
Diuretic	280; 62% (57% to 66%) Missing data=2	203; 65% (60% to 71%) Missing data=2	77; 54% (46% to 62%) Missing data=0	0.02
Statin	237; 52% (48% to 57%) Missing data=1	161; 52% (46% to 57%) Missing data=1	76; 53% (45% to 61%) Missing data=0	0.78

Continued

**Table 1** Continued

	Overall Overall (N=455)	By region		p Value
		Australia and NZ (N=312)	SE Asia (N=143)	
Antiplatelet agent	226; 50% (45% to 54%) Missing data=2	148; 48% (42% to 53%) Missing data=2	78; 55% (46% to 62%) Missing data=0	0.18
β-blocker	224; 49% (45% to 54%) Missing data=2	160; 52% (46% to 57%) Missing data=2	64; 45% (37% to 53%) Missing data=0	0.18
ACE inhibitor/angiotensin receptor blocker	217; 48% (43% to 53%) Missing data=3	161; 52% (47% to 58%) Missing data=3	56; 39% (32% to 47%) Missing data=0	0.01
Long-acting oral anticoagulant	127; 28% (24% to 32%) Missing data=3	105; 34% (29% to 39%) Missing data=3	22; 15% (10% to 22%) Missing data=0	<0.0001
Calcium channel blocker	112; 25% (21% to 29%) Missing data=3	74; 24% (20 to 29%) Missing data=3	38; 27% (20 to 34%) Missing data=0	0.54
Inhaled β-sympathomimetic	103; 23% (19% to 27%) Missing data=4	85; 28% (23% to 33%) Missing data=4	18; 13% (8% to 19%) Missing data=0	0.0004
Nitrate	85; 19% (16% to 23%) Missing data=4	51; 17% (13% to 21%) Missing data=4	34; 24% (18% to 31%) Missing data=0	0.07
Insulin	66; 15% (12% to 18%) Missing data=4	46; 15% (11% to 19%) Missing data=4	20; 14% (9% to 21%) Missing data=0	0.79
Aldosterone antagonist	54; 12% (9% to 15%) Missing data=3	39; 13% (9% to 17%) Missing data=3	15; 10% (6% to 17%) Missing data=0	0.51
Oral corticosteroid	22; 5% (3% to 7%) Missing data=5	17; 6% (3% to 9%) Missing data=5	5; 4% (2% to 8%) Missing data=0	0.35
Home oxygen	16; 4% (2% to 6%) Missing data=4	14; 5% (3% to 7%) Missing data=4	2; 1% (0.5% to 5%) Missing data=0	0.09

Data adjusted for missing data.

AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease; NZ, New Zealand; PE, pulmonary embolism; SE Asia, South East Asia, combined data from Malaysia, Hong Kong and Singapore.

**Table 2** Examination findings, testing and pathology findings, overall and by region

	Overall	By region		p Value
	Overall (N=455)	Australia and NZ (N=312)	SE Asia (N=143)	
<b>Examination findings in ED</b>				
Pulse (bpm)	86 (72–102) Missing data=6	85 (71–102) Missing data=4	90 (73–103) Missing data=2	0.36
SBP (mm Hg, IQR)	143 (125–166) Missing data=8	141 (122–160) Missing data=7	144 (128–172) Missing data=1	0.08
Respiratory rate (per min, IQR)	24 (20–28) Missing data=4	24 (20–30) Missing data=4	21 (19–26)	0.0007
Oxygen saturation on air (%; where known, IQR)	95% (92–98%) Missing data=113	94% (90–96%) Missing data=76	97% (95–99%) Missing data=37	<0.0001
Oxygen saturation on oxygen (%; where known excludes patients with SpO <sub>2</sub> on air, IQR)	97% (95–99%) Missing data=5	97% (94–99%) Missing data=4	98% (97–100%) Missing data=1	<0.0001
Peripheral oedema (N, %, 95% CI)	301; 77% (72% to 81%) Missing data=63	204; 76% (71% to 81%) Missing data=45	97; 78% (70% to 84%) Missing data=18	0.68
SBP>140 mm Hg (N, %, 95% CI)	235; 53% (48% to 57%) Missing data=8	156; 52% (46% to 57%) Missing data=7	79; 56% (47% to 64%) Missing data=1	0.41
SBP>160 mm Hg (N, %, 95% CI)	126; 28% (24% to 33%) Missing data=8	76; 25% (20% to 30%) Missing data=7	50; 35% (28% to 43%) Missing data=1	0.03
SpO <sub>2</sub> <90%, (on air or oxygen) (N, %, 95% CI)	74; 16% (13% to 20%) Missing data=5	56; 18% (14% to 23%) Missing data=4	8; 6% (3% to 11%) Missing data=1	0.007
Respiratory rate >30/min, (N, %, 95% CI)	76; 17% (14% to 21%) Missing data=4	63; 20% (16% to 25%) Missing data=4	16; 12% (7% to 17%) Missing data=0	0.02
<i>Chest findings in ED</i>				
Basal crepitations	N, % (95% CI) 233; 53% (49% to 58%) Missing data=19	N, % (95% CI) 146; 49% (44% to 55%) Missing data=15	N, % (95% CI) 87; 63% (54% to 70%) Missing data=4	0.01
Widespread crepitations	86; 20% (16% to 24%) Missing data=19	67; 23% (18% to 28%) Missing data=15	19; 14% (8% to 20%) Missing data=4	0.05
<i>Testing ordered in ED</i>				
Chest radiograph	N, % (95% CI) 429; 95% (92% to 96%) Missing data=0	N, % (95% CI) 292; 94% (90% to 96%) Missing data=0	N, % (95% CI) 137; 96% (91% to 98%) Missing data=0	0.48
Lung ultrasound in ED	3; 0.7% (0.2% to 2%) Missing data=0	1; 0.3% (0.06% to 2%) Missing data=0	1% (0.4% to 5%) Missing data=0	0.19
Echocardiography in ED	10; 2% (1% to 4%) Missing data=2	7; 2% (1% to 5%) Missing data=2	3; 2% (0.7% to 6%) Missing data=0	0.91
Electrolytes	393; 86% (83% to 89%) Missing data=0	299; 98% (96% to 98%) Missing data=0	94; 66% (58% to 73%) Missing data=0	<0.0001
Full blood examination	408; 90% (87% to 92%) Missing data=0	305; 98% (95% to 99%) Missing data=0	103; 72% (64% to 79%) Missing data=0	<0.0001
BNP (N, %, 95% CI)	25; 5% (4% to 8%) Missing data=0	25; 8% (5% to 12%) Missing data=0	0; 0% (0% to 2.6%) Missing data=0	0.001
NT-proBNP	62; 14% (11% to 17%) Missing data=0	33; 11 (8% to 14%) Missing data=0	29; 20% (15% to 28%) Missing data=0	0.008

Continued

Table 2 Continued

	Overall	By region		p Value
	Overall (N=455)	Australia and NZ (N=312)	SE Asia (N=143)	
Natriuretic peptide (either BNP or NT-proBNP)	87; 19% (16% to 23%) Missing data=0	58; 19% (15% to 23%) Missing data=0	29; 20% (15% to 28%) Missing data=0	0.76
Troponin	287; 63% (59% to 67%) Missing data=0	204; 65% (60% to 70%) Missing data=0	83; 58% (50% to 66%) Missing data=0	0.16
C reactive protein	145; 32% (28% to 36%) Missing data=0	140; 45% (40% to 50%) Missing data=0	5; 4% (2% to 8%) Missing data=0	<0.0001
Blood gas analysis	167; 37% (32% to 41%) Missing data=0	145; 46% (41% to 52%) Missing data=0	22; 15% (10% to 22%) Missing data=0	<0.001
Glucose	256; 56% (52% to 61%) Missing data=0	191; 61% (56% to 66%) Missing data=0	65; 45% (38% to 54%) Missing data=0	0.002
D-dimer	11; 2% (1% to 4%) Missing data=0	11; 4% (2% to 6%) Missing data=0	0; 0% (0% to 3%) Missing data=0	0.04
Lactate	125; 27% (24% to 32%) Missing data=0	108; 35% (30% to 40%) Missing data=0	17; 12% (8% to 18%) Missing data=0	<0.0001
Albumin	256; 56% (52% to 61%) Missing data=0	221; 71% (66% to 76%) Missing data=0	35; 24% (18% to 32%) Missing data=0	<0.0001
Pathology findings	<i>N, % (95% CI)</i>	<i>N, % (95% CI)</i>	<i>N, % (95% CI)</i>	
Serum sodium concentration <130 mmol/L	18; 4% (3% to 6%) Missing data=0	15; 5% (3% to 8%) Missing data=0	3; 2% (0.7% to 6%) Missing data=0	0.20
Haemoglobin <10 mmol/L	67; 15% (12% to 18%) Missing data=0	48; 15% (12% to 20%) Missing data=0	19; 13% (9% to 20%) Missing data=0	0.57
Serum creatinine >80 µmol/L	313; 69% (65% to 73%) Missing data=0	229; 73% (68% to 78%) Missing data=0	84; 59% (51% to 66%) Missing data=0	0.002
Serum creatinine >150 µmol/L	114; 25% (21% to 29%) Missing data=0	80; 26% (21% to 31%) Missing data=0	34; 24% (18% to 31%) Missing data=0	0.73
Troponin >99th centile for test	173; 38% (34% to 43%) Missing data=0	123; 39% (34% to 45%) Missing data=0	50; 35% (28% to 43%) Missing data=0	0.41

Data adjusted for missing data.

BNP, β natriuretic peptide; bpm, beats per minute; ED, emergency department; NT-proBNP, N-terminal pro β natriuretic peptide; NZ, New Zealand; SBP, systolic blood pressure; SE Asia, South East Asia, combined data from Malaysia, Hong Kong and Singapore; SpO<sub>2</sub>, oxygen saturation by pulse oximetry.

**Table 3** Treatment and outcomes, overall and by region

	Overall	By region		p Value
	Overall (N=455)	Australia and NZ (N=312)	SE Asia (N=143)	
Treatment in ED	<i>N, % (95% CI)</i>	<i>N, %, (95% CI)</i>	<i>N, %, (95% CI)</i>	
Oxygen	285; 62% (58% to 67%)	186; 60% (54% to 65%)	99; 69% (61% to 76)	0.06
Non-invasive ventilation	56; 12% (10% to 16%)	49; 16% (12% to 20%)	7; 5% (2% to 10%)	0.002
Mechanical ventilation	4; 1% (0.3% to 2%)	2; 0.6% (0.1% to 2.3%)	2; 1% (0.4% to 5%)	0.81
Diuretic				
Any	332; 73% (69% to 77%) Missing data=2	236; 76% (71% to 81%) Missing data=2	96; 67% (59% to 74%) Missing data=0	0.06
IV	303; 67% (62% to 71%) Missing data=2	210; 68% (62% to 73%) Missing data=2	93; 65% (57% to 72%) Missing data=0	0.65
Oral	46; 10% (8% to 13%) Missing data=2	40; 13% (10% to 17%) Missing data=6	6; 4% (2% to 9%) Missing data=0	0.007
Nitrate				
Any	115; 25% (22% to 30%) Missing data=2	72; 23% (19% to 28%) Missing data=2	43; 30% (23% to 38%) Missing data=0	0.15
IV bolus	1; 0.2% (0.04% to 1%) Missing data=2	1; 0.3% (0.06% to 2%) Missing data=2	0; 0% (0% to 3%) Missing data=0	0.69
IV infusion	31; 7% (5% to 10%) Missing data=3	16; 5% (3% to 8%) Missing data=3	15; 10% (6% to 17%) Missing data=0	0.06
Sublingual/transdermal/oral	89; 20% (16% to 24%) Missing data=4	58; 19% (15% to 24%) Missing data=4	31; 22% (16% to 29%) Missing data=0	0.56
Inotrope/vasopressor	5; 1% (0.5% to 3%) Missing data=5	4; 1% (0.5% to 3%) Missing data=5	1; 0.7% (0.1% to 4%) Missing data=0	0.92
Morphine	16; 4% (2% to 6%) Missing data=6	14; 5% (3% to 8%) Missing data=6	2; 1% (0.4% to 5%) Missing data=0	0.16
Anticoagulant	31; 7% (5% to 10%) Missing data=5	26; 8% (6% to 12%) Missing data=5	5; 4% (2% to 8%) Missing data=0	0.08
Antiplatelet agent	40; 9% (7% to 12%) Missing data=5	28; 9% (6% to 13%) Missing data=5	12; 8% (5% to 14%) Missing data=0	0.92
Antibiotic	71; 16% (13% to 19%) Missing data=5	59; 19% (15% to 24%) Missing data=5	12; 8% (5% to 14%) Missing data=0	0.005
Systemic corticosteroid	26; 6% (4% to 8%) Missing data=5	25; 8% (6% to 12%) Missing data=5	1; 0.7% (0.1% to 4%) Missing data=0	0.003
Inhaled bronchodilator	58; 13% (10% to 16%) Missing data=5	49; 16% (12% to 20%) Missing data=5	9; 6% (3% to 11%) Missing data=0	0.007
Treatment combinations	<i>N, % (95% CI)</i>	<i>N, % (95% CI)</i>	<i>N, % (95% CI)</i>	
Diuretic+nitrate (any route)	97; 21% (18% to 25%) Missing data=2	59; 19% (15% to 24%) Missing data=2	38; 27% (20% to 34%) Missing data=0	0.09
Diuretic+inhaled bronchodilator	47; 10% (8% to 14%) Missing data=5	41; 13% (10% to 18%) Missing data=5	6; 4% (2% to 9%) Missing data=0	0.005
Diuretic+antibiotic	58; 13% (10% to 16%) Missing data=5	48; 16% (12% to 20%) Missing data=5	10; 7% (4% to 12%) Missing data=0	0.02

Continued



Table 3 Continued

	Overall	By region		p Value
	Overall (N=455)	Australia and NZ (N=312)	SE Asia (N=143)	
Diuretic+nitrate (any route)+antibiotic	18; 4% (3% to 6%) Missing data=6	15; 5% (3% to 8%) Missing data=6	3; 2% (0.7% to 6%) Missing data=0	0.25
Diuretic+inhaled bronchodilator+systemic corticosteroid	13; 3% (2% to 5%) Missing data=5	13; 4% (2% to 7%) Missing data=5	0; 0% (0% to 3%) Missing data=0	0.03
Diuretic+inhaled bronchodilator+systemic corticosteroid+antibiotic	8; 2% (1% to 4%) Missing data=5	8; 3% (1% to 5%) Missing data=5	0; 0% (0% to 3%) Missing data=0	0.12
Outcome	<i>N, % (95% CI)</i>	<i>N, % (95% CI)</i>	<i>N, % (95% CI)</i>	
Admission to hospital ward (including ICU and interhospital transfers for admission)	392; 86% (83% to 89%) Missing data=1	265; 85% (81% to 89%) Missing data=1	127; 89% (83% to 93%) Missing data=0	0.37
ICU admission	19; 4% (3% to 7%) Missing data=1	13; 4% (3% to 7%) Missing data=1	6; 4% (2% to 9%) Missing data=0	0.81
ED short stay unit management (excludes hospital ward admission)	10; 2% (1% to 4%) Missing data=1	6; 2% (1% to 4%) Missing data=1	4; 3% (1% to 7%) Missing data=0	0.81
Length of stay for patients admitted to hospital (days, median, IQR)	6, 4 to 9 Missing data=22	6, 3 to 9 Missing data=22	6, 3 to 8 Missing data=0	0.44
Died in ED	2; 0.5% (0.1% to 2%) Missing data=1	2; 0.6% (0.2% to 2%) Missing data=1	0; 0% (0% to 3%) Missing data=0	0.58
In-hospital mortality for patients admitted to ward including ICU	20; 5% (3% to 7%) Missing data=22	14; 6% (3% to 9%) Missing data=22	6; 5% (2% to 10%) Missing data=0	0.92

Data adjusted for missing data.

Nitrate: some patients had more than one route of administration.

ED, emergency department; ICU, intensive care unit; IV, intravenous; NZ, New Zealand; SE Asia, South East Asia, combined data from Malaysia, Hong Kong and Singapore.



patients had chest findings of fluid overload on auscultation (73%) or peripheral oedema (77%). The cohort of South East Asian patients was less likely to have oxygen saturations (on air or oxygen) <90% (6% vs 18%,  $p=0.007$ ) or a respiratory rate >30/min (12% vs 20%,  $p=0.02$ ) on presentation.

### Investigations

Ordered investigations are shown in table 2. Chest radiograph (chest X-ray) was performed in 95%, troponin concentration in 63%, blood gas (either arterial or venous) in 37%, C reactive protein (CRP) in 32%, natriuretic peptide (NP) level (N-terminal pro  $\beta$  natriuretic peptide (NT-proBNP) or BNP) in 19% and D-dimer in 2%. Lung ultrasound (<1%) and echocardiography (2%) were uncommonly conducted in ED. Overall, anaemia (haemoglobin <10 mmol/L, 15%) and hyponatraemia (sodium concentration <130 mmol/L, 4%) were relatively infrequent findings.

South East Asian sites had significantly lower rates of ordering both routine tests (such as full blood count (72% vs 98%,  $p<0.001$ ) and electrolytes (66% vs 98%,  $p<0.001$ )) as well as tests targeting more specific conditions (such as blood gas (15% vs 46%,  $p<0.001$ ), CRP (4% vs 45%,  $p<0.001$ ) and lactate (12% vs 35%,  $p<0.001$ )).

### Treatment

Table 3 describes treatment modalities used, which included non-invasive ventilation (12%), diuretics (73%) and nitrates (25%). In line with the very low number of patients with a systolic blood pressure <90 mm Hg, the use of inotropes was infrequent overall (<1%). One hundred and fifty-five (34%, 95% CI 30% to 39%) patients received antibiotics, inhaled  $\beta$ -agonists or corticosteroids, suggesting either mixed disease or diagnostic uncertainty. Treatment combinations covering for more conditions than HF alone were less common in South East Asian EDs.

### Outcomes

Outcomes are summarised in table 3. Most patients (86%) were admitted to hospital with a median LOS of 6 days (IQR 4–9), including a 4% admission rate to the ICU. Very few patients (2%) were admitted to an ED short stay setting. This admission rate pattern, including LOS, was similar across geographic areas. Hospital diagnosis was concordant with ED diagnosis in 81% of cases, with discordant cases mainly accounted for by hospital discharge diagnosis of COPD (4%), pulmonary infection (4%) and acute coronary syndrome (3%). In-hospital mortality (including deaths in ED) was 5.1% (95% CI 3.3% to 7.7%) and was similar between regions.

## DISCUSSION

### Summary

In the Asia Pacific region, HF is a common diagnosis in patients presenting to the ED with a principal symptom

of dyspnoea with the majority (86%) of these patients admitted to hospital, a proportion in keeping with other international cohorts.<sup>10</sup> This unique study of breathless patients in the ED highlights some significant regional differences in the demographic and clinical features on presentation, ordered investigations and treatment of patients with acute HF.

### Comparison with existing literature

The outcomes of patients with HF compare favourably with other registries, despite our cohort being older and compliance with certain features of evidence-based guidelines seemingly suboptimal. The median LOS was 6 days, at the lower end of ranges reported by other studies of between 3.5 and 20 days.<sup>11 12</sup> In-hospital mortality was 5.1%, at the lower end of the reported median range of 4–30%.<sup>2</sup> There was infrequent use of ED short stay admission for this patient group, reflecting an almost dichotomous disposition pathway (inpatient admission vs discharge); however, others have suggested that up to half of the ED patients with HF could be safely discharged after a brief period of observation.<sup>13</sup> This suggests a missed opportunity in our cohort where short stay wards in ED are usually available. It is possible that a number of inpatient admissions could have been avoided if appropriate local short stay pathways existed.

With a median age of 79 years, patients in our cohort were older than patients in the three largest (US) registries (ADHERE; OPTIMIZE-HF; GWTG-HF 72–74 years)<sup>14–17</sup> and several of the smaller (European and Japanese) registries (EHFS, ESC-HF, IN-HF, EFICA, RO-AHFS, ATTEND; ranging from 69 to 73 years).<sup>2</sup> Gender distribution was similar to the three US registries.

Overall patient demographics and comorbidities were comparable with those reported in existing HF registries in the USA and Europe; however, there was considerable regional variation for these variables within our cohort. South East Asian patients were younger than their Australian and New Zealand counterparts; however, they had similar rates of cardiovascular comorbidities (diabetes, ischaemic heart disease, hypertension, dyslipidaemia). Lower rates of pre-existing HF, valvular disease and COPD in the South East Asian patients may be due to their being a median 8 years younger. Our finding is consistent with previous data showing that South East Asian patients with HF are younger, suggesting that ethnicity may play a part.<sup>18</sup> Differences in mode of presentation between South East Asian patients and their Australian and New Zealand counterparts, with less ambulance usage in South East Asian patients, may be due to the younger age, fewer comorbidities and lower rates of hypoxia or tachypnoea, or to regional differences in ambulance availability, use and cost. Despite these differences, admission rates and hospital LOS were similar in the different geographical regions.

Our findings of one in five patients overall having an NP ordered is lower than that expected from acute HF

guidelines<sup>6</sup> and difficult to compare to other cohorts due to a lack of data collection or large number of missing data in those cohorts. The National Institute for Health and Care Excellence (NICE) guidelines for acute HF<sup>5</sup> recommends using NT-proBNP in patients with suspected new-onset acute HF. Although more than half of our cohort had a previous diagnosis of HF, the overall use of NPs is lower than recommended. It is possible that NPs were mainly used for patients in whom there was diagnostic uncertainty. Some hospitals have test ordering protocols that defer this test ordering to inpatient teams. Using NPs to titrate management in patients with chronic HF is associated with improved mortality,<sup>19 20</sup> but it is unclear if the timing of this measurement matters (ED vs inpatient). Although our study highlights a gap between guidelines and implementation of evidence-based testing in clinical care, it raises a question about the specificity and applicability of these guidelines to our ED setting, since the outcomes of our study compare favourably despite the low NP ordering rates.

There were significant differences in the number of investigations requested for each patient assessed with an ED diagnosis of HF. Overall, patients presenting to Australian EDs had the most pathology tests ordered, with South East Asian EDs the least. This could possibly be explained by the South Asian cohort being younger, having fewer comorbidities, and as such, alternative diagnoses may not have needed to be entertained as frequently. Other regional differences in test ordering could be explained by different levels of perceived medicolegal risk, varying approaches to investigations either clinically or logistically influenced by training programmes, time targets, testing bundles, insurance systems and out-of-pocket expenses. Lower levels of anaemia and hyponatraemia were detected in comparison to other registries and may be due to differences in the chosen cut-offs defining abnormalities (we did not include mild hyponatraemia (130–135 mmol/L)], eg). Overall, over one-third of patients (37%) had a blood gas ordered, where approximately one-sixth of patients were hypoxic (16%). We cannot comment on whether blood gases were ordered for assessment of ventilation or for other reasons such as the (bedside) assessment of acid–base disorders or electrolyte status.

Three-quarters of patients were treated with diuretics and one-quarter with nitrates, with relatively little geographical variation. Diuretic treatment was less commonly initiated compared with other registries (73% vs 76–92%—ADHERE 92%, EHFS II—82%, ATTEND 76%, ALARM 90%)<sup>2</sup> and less than guidelines would suggest—since they are recommended as first-line treatment.<sup>5 21</sup> The proportion of nitrates used is somewhat more in line with guidelines, which suggest that nitrates should not be routinely offered<sup>5</sup> or as an adjunct if hypotension is absent.<sup>6</sup>

Despite the seemingly suboptimal adherence to components of the guidelines in terms of investigations (NP

ordering) and treatments (diuretic use), patient outcomes are favourable compared with other registries, which raises questions about the utility of the existing guidelines in undifferentiated patients presenting to the ED with dyspnoea. Other treatments and treatment combinations did vary considerably, with South East Asian patients receiving fewer antibiotics,  $\beta$ -agonists and corticosteroids. As outlined previously, this is possibly a function of this cohort being younger with more commonly single-system disease. Overall, one in six patients received antibiotics (16%), which may be a reflection of the proportion of patients being judged by the treating clinician to have mixed disease (including infection), although we are unable to comment on the appropriateness of its use.

Very few (~1%) patients received inotropic support compared with registries reporting use between 15% and 30% (ADHERE 15%, EHFS II 30%, ATTEND 18%, ALARM 22%).<sup>2</sup> This finding suggests regional practice variation that seems unlikely to be due to difference in HF severity (since our cohort was older with similar clinical features and comorbidities). This may be partially explained by the 19% of patients with a discordant ED and hospital diagnosis. Another possible explanation is that since the patients in our cohort had dyspnoea as a main symptom, they were more likely to have HF with preserved ejection fraction (EF) and, as such, less likely to require inotropic support. In any case, this difference in inotrope use could have implications for interpretations of our outcomes, since even short-term inotrope use has been associated with increased mortality.<sup>22</sup>

### Strengths and limitations

The study sites were located in the South East Asia/Australasia geographical area and may not be generalisable to other regions. The results of the South East Asia cohort were based on nine sites in three countries (Hong Kong, Singapore and Malaysia), and our finding may not be able to be extrapolated to other countries in South East Asia.

Although we collected data prospectively from consecutive patients presenting with dyspnoea, it is possible that patients with HF were missed due to the design of the overarching study which focused on including patients with dyspnoea as a main symptom. Over 90% of patients with HF have dyspnoea,<sup>23</sup> but it is possible that a proportion of patients with HF may have presented without dyspnoea—and rather chest pain, fatigue or peripheral oedema.

The ED diagnosis of HF was based on clinician judgement. Since there is no gold standard for the diagnosis of HF, clinician diagnosis of HF based on the history, signs of fluid overload on physical examination and/or chest radiograph ( $\pm$  response to HF therapy) are often an accepted standard.<sup>24</sup> The agreement between ED and final hospital diagnosis was 81%, suggesting good accuracy of diagnosis. In some of the discordant cases, where the primary hospital diagnosis was COPD (4%),

pulmonary infection (4%) or acute coronary syndrome (3%), HF may have been a secondary process. Targeted use of lung ultrasound<sup>25</sup> and/or bedside echocardiography and NPs could possibly further improve the diagnostic accuracy in ED.<sup>26</sup>

Echocardiography was rarely performed in the ED, in line with the recent recommendation that urgent echo in the ED is only required when the patient is in cardiogenic shock.<sup>27</sup> As a result, data on EF were not collected in the vast majority of patients and we cannot comment on proportions of patients with preserved or reduced EF. This makes interpretation regarding adherence to some components of the guidelines related to EF difficult, but it highlights the scope for inclusion of specific ED populations with both preserved and reduced EF in future guidelines.

## CONCLUSION

This study on patients with HF provides a novel insight in several ways, highlighting regional variation in demographics, investigations and treatment in a cohort of patients from a previously under-reported geographical area, the Asia Pacific region. Overall, despite an older cohort, and a seemingly suboptimal adherence to the guidelines in terms of investigations and treatments, patient outcomes are favourable compared with other registries.

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