Heart failure (HF) is a common, costly, disabling, and potentially deadly condition. It is the leading cause of hospitalization in people aged ≥65 years. HF is an increasing important global public health issue, particularly in aging societies such as Hong Kong. HF is associated with significantly reduced physical and mental health, resulting in a markedly decreased quality of life. As a result of the costs of hospitalization, it is also associated with high health expenditure, accounting for ≈2% of all healthcare expenditure. Coronary artery disease, valvular heart disease, hypertension, overweight, and diabetes mellitus are the main causes and risk factors of HF. Despite the impressive number of effective treatments available, patients with HF continue to experience progressively worsening symptoms, frequent admission to hospital, and premature death. So studies are required to help decision-makers target resources toward implementing the prevention, which is of most importance for the elderly population.

Clinical Perspective on p 935

Background—Although the seasonal variation and the effect of cold temperature on heart failure (HF) morbidity have been well documented, it is unknown whether the temperature variation within a day, that is, diurnal temperature range (DTR), is an independent risk factor for HF. We hypothesized that large DTR might be a source of additional environmental stress and, therefore, a risk factor for HF exacerbation. We aimed to test the association between DTR and HF hospitalization and to examine the effect modifiers, such as age, sex, and season.

Methods and Results—We collected daily meteorologic data and emergency HF hospital admissions from 2000 to 2007 in Hong Kong. We used Poisson regression models to fit the relationship between daily DTR and emergency HF hospitalizations, after adjusting for the time trend, seasonality, mean temperature, humidity, and levels of outdoor air pollution. We confirmed the seasonal variation of HF with peak hospital admissions in winter in Hong Kong. The adverse effects of DTR on emergency HF admissions were observed on the current day and lasted for the following several days. Every 1°C increase of DTR at lag0 corresponded to 0.86% (95% confidence interval, 0.31%–1.43%) increment of emergency hospital admissions for HF. DTR exhibited significantly greater effect in the cool season, and on female and elderly patients.

Conclusions—Greater temperature change within a day was associated with increased emergency hospital admissions for HF. Health policymakers and hospitals may want to take into account the increased demand of specific facilities for susceptible population in winter with greater daily temperature variations. (Circ Heart Fail. 2013;6:930-935.)

Key Words: diurnal temperature range ■ emergency hospital admission ■ heart failure ■ temperature variation ■ time series study
effective thermoregulation and may be more sensitive to the temperature change.\textsuperscript{20} Patients with HF showed much higher hospital admissions in the winter months, which lead us to examine the association between DTR and HF hospitalization varied by season.

Hong Kong is situated on the south coast of China. With a land area of 1104 km\(^2\) and a population of 7 million people, it is one of the most densely populated areas in the world. Hong Kong has a subtropical climate with hot and humid summer and moderate cool winter. The mean temperature is 27.6°C from May to October (the warm season) and 19.5°C from November to April (the cool season). HF in Hong Kong is common and increasing according to the information from Hospital Authority (the statutory body running all public hospitals in Hong Kong: http://www.ha.org.hk). In this study, we aimed to test the associations between DTR and HF hospitalizations in Hong Kong and to study the effect modifiers, such as age, sex, and season.

\section*{Methods}

\subsection*{Data Collection}

This is an ecological study using time series analysis. We collected city-wide hospital admissions for all circulatory diseases and HF from January 2000 to December 2007 in Hong Kong. The hospital admission data were taken from the publicly funded hospitals providing 24-hour accident and emergency services and covering 90% of hospital beds in Hong Kong for local residents.\textsuperscript{8} The patient data captured from the computerized medical record system included age, sex, date of admission, source of admission, and principal diagnosis on discharge coded with International Statistical Classification of Diseases, Ninth Revision (ICD-9). We abstracted the hospital admissions through the accident and emergency services for diseases of the circulatory system (ICD-9: 390–459) and HF (ICD-9: 428). We also computed the emergency HF admissions by sex and by age groups (<65, 65–74, and ≥75 years) as the health outcomes. Daily admissions for influenza (ICD-9: 487) were used to identify influenza epidemics, which were then treated as a potential confounder in the data analysis.\textsuperscript{21} The present study used grouped health information (number of emergency hospital admissions on each day) collected on a routine basis in the public hospital system provided by the Hospital Authority, no specific institutional review committee approval and informed consents from subjects were required, as information on individuals was not involved.

We collected the meteorologic information, including the daily maximum, minimum, mean temperature, and relative humidity, for the same period from the Hong Kong Observatory. DTR was calculated by the maximum temperature minus the minimum temperature within the same day.

As air pollutants have been identified as risk factors for emergency HF hospitalizations,\textsuperscript{6,9} we also collected the air pollution concentrations from the Environmental Protection Department. Hourly concentrations of 4 criteria air pollutants (particles with an aerodynamic diameter <10 \(\mu\)m, PM\textsubscript{10}, nitrogen dioxide, NO\textsubscript{2}, ozone, O\textsubscript{3}, and sulfur dioxide, SO\textsubscript{2}) monitored in 10 general stations were used to generate daily mean air pollution concentrations to denote the pollution level in Hong Kong.\textsuperscript{22}

\subsection*{Statistical Modeling}

Generalized additive Poisson regression models were used to fit the relationship between the daily DTR and the emergency HF hospitalizations. We used the smoothing spline, \(s(.)\), to filter out seasonal patterns and long-term trends in daily hospitalizations, as well as the daily mean temperature and relative humidity.\textsuperscript{23} We also included an adjustment for the day of the week and dichotomous variables, such as public holidays and influenza outbreaks.

We followed previous studies to select a priori the model specification and the \(df\) for the time trend and other meteorologic variables.\textsuperscript{22–24} We used a \(df\) of 8/\(y\) for the time trend, a \(df\) of 6 for the mean temperature of the current day (\(\text{Temp}_0\)) and the previous 3 days’ moving average (\(\text{Temp}_{0,0}\)), and a \(df\) of 3 for the current day relative humidity (\(\text{Humid}_0\)). We included the day of the week (DOW) and public holidays (Holiday) in the model as dummy variables.\textsuperscript{25} To adjust for the confounder effect of an influenza epidemic on emergency hospital admissions, we entered a dummy variable for the weeks with several influenza hospital admissions exceeding the 75 percentile in a year into the core model.\textsuperscript{26}

Briefly, we set up a core model to remove the long-term trends, seasonal variations, and adjust for time varying confounders as follows:

\begin{equation}
\log(E(Y)) = \alpha + s(t, df = 8/\(y\) \times \text{no.of years}) + s(\text{Temp}_0, df = 6) + s(\text{Temp}_{0,0}, df = 6) + s(\text{Humid}_0, df = 3) + \beta_1 \text{DOW} + \beta_2 \text{Holiday} + \beta_3 \text{influenza,}
\end{equation}

where \(E(Y)\) is the expected daily emergency HF hospital admission counts on day \(t\) and \(s(.)\) is the smoothing spline function for nonlinear variables. We examined the residuals of the core model to check whether there were discernible patterns and autocorrelation by means of residual plot and partial autocorrelation function plot. The partial autocorrelation function of residuals of the core model (Equation 1) was <0.1 for all the lags, which meant no serial correlation in the residuals and sufficient confounder control.\textsuperscript{27} No discernible patterns and no autocorrelation in the residuals are the criteria for an adequate core model set up, which is intended to remove all potential confounders in the daily variations of health outcome. The linear effect of DTR on emergency HF admissions was then estimated for the same day and ≤5 days before the outcome (single-lag effect from lag\(_g\) to lag\(_r\)). The overall cumulative effect of DTR lasting for 0 to 5 days was estimated by distributed lag model.\textsuperscript{28} To justify the assumption of linearity between the logarithm of emergency HF hospital admissions and DTR, we graphically examined the dose–response relationship derived using a smoothing function.\textsuperscript{26} Sensitivity analyses were conducted to test such association by further adjusting for the confounding effects from air pollution. Sensitivity analysis was also conducted to test whether the DTR effect is stable by replacing the mean temperature with the minimum temperature in core model (Equation 1).

In addition to the whole period analysis, we examined the effect of DTR for the warm season (from May to October) and the cool season (November to April) separately, using half the \(df\) of 4/\(y\) for the time trend.\textsuperscript{29} Modified effects of sex and age group were also examined using subgroup analyses of HF hospitalizations as the health outcomes.\textsuperscript{30} We tested the statistical significance of differences among season, sex, or age group by calculating \((\hat{\beta}_s - \hat{\beta}_d)/\sqrt{SE_s^2 + SE_d^2}\), where \(\hat{\beta}_s\) and \(\hat{\beta}_d\) are the estimates for the 2 categories (eg, warm and cool season or women and men), and \(SE_s\) and \(SE_d\) are their respective standard errors.\textsuperscript{20–24} A factor >1.96 was considered as statistically significant difference at \(\alpha=0.05\) level.

The results were expressed in terms of the percentage increase (excess relative risk, %) in emergency HF hospital admissions for 1°C increase of DTR and respective 95% confidence intervals (CIs). All analyses were conducted in the statistical environment R2.15.1 (R Development Core Team, 2012: http://www.r-project.org).

\section*{Results}

\subsection*{Data Description}

From 2000 to 2007, there has been ≈20% increase in hospital admissions for HF. The emergency admissions for HF were 11066 in 2000, whereas this number increased to 13290 in 2007. During our study period, a total of 95897 emergency hospital admissions for HF were recorded in our study population, accounting for ≈21% of emergency hospitalizations because of total circulatory diseases. On average there were 33 emergency admissions per day for HF, of which ≈56.4%
were women. The percentage of HF hospitalizations were 10.4%, 22.9%, and 66.8% in the 3 age groups (<65, 65–74, and ≥75 years), respectively. The daily mean emergency HF admissions were significantly higher in the cool season than those in the warm season (39 versus 27; t test: P value <0.01; (Table 1). The daily mean air temperature was 23.6°C with a mean DTR of 4.0°C. The daily mean concentration of air pollutants was 53.6, 57.8, 41.6, and 20.3 μg/m³ for PM₁₀, NO₂, O₃, and SO₂, respectively.

Regression Results
Figure 1 shows the time series of the daily count of observed HF hospitalizations (a typical seasonal variation with peak admissions in winter months) and the predicted values fitted by the Poisson regression core model. Dose–response curve (Figure 2) shows that the association between the risk of emergency HF hospitalizations and DTR was essentially linear. The adverse effects of DTR on emergency HF admissions were observed in our study for all the lags we examined, after adjusting for the time trend, seasonality, absolute air temperature, calendar effect, and influenza epidemics. Every 1°C increase of DTR at lag₀ corresponded to 0.86% (95% CI, 0.31%–1.43%) increase of emergency hospital admissions for HF. The overall cumulative effect of DTR lasting for 0–5 days was associated with 3.76% (95% CI, 3.36%–4.16%) increment of emergency HF hospitalizations. The effects were significantly higher in the cool season than those in warm season at lag₁, lag₂, and 5-day distributed lags (Figure 3).

Further adjustment for the possible confounding effects from air pollutants at the same lags resulted in decreased excess relative risk in general, especially when adjusted for NO₂, although the cumulative effect of DTR was still statistically significant (Table 2). Replacing the terms of mean temperature with the minimum temperature in core model (Equation 1) showed that the association between DTR and HF hospitalizations was also robust to the adjustment for daily minimum temperature (Table 2).

Stratified analyses by sex (Table 3) showed that DTR exposure exhibited greater effect on female patients with HF than on male patients with HF, with the cumulative effect estimates of 4.41% (95% CI, 3.89%–4.92%) and 2.93% (95% CI, 2.37%–3.50%) increase of HF admissions per 1°C increase of DTR, respectively. At the same time, DTR exposure exhibited greater effect on patients aged ≥75 years; the corresponding cumulative effect size was 4.13% (95% CI, 3.66%–4.60%) per 1°C increase of DTR (Table 3). Results demonstrated that

| Table 1. Distribution of Emergency HF Hospital Admissions, Meteorologic Factors, and Air Pollution Concentrations in Hong Kong, 2000–2007 (2922 Days) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Emergency hospital admissions (counts/d) | Mean | SD | Min. | P₁₀ | P₅₀ | P₇₅ | Max. |
| All circulatory diseases | 156.1 | 23.7 | 66 | 141 | 155 | 171 | 243 |
| Heart failure | 32.8 | 10.8 | 10 | 25 | 31 | 39 | 86 |
| In cool season | 39.2 | 10.8 | 15 | 32 | 38 | 46 | 86 |
| In warm season | 26.6 | 6.1 | 10 | 22 | 26 | 30 | 49 |
| Women | 18.5 | 6.7 | 4 | 14 | 18 | 22 | 57 |
| Men | 14.3 | 5.6 | 2 | 10 | 13 | 17 | 41 |
| Age, y | | | | | | | |
| <65 | 3.4 | 2 | 0 | 2 | 3 | 5 | 12 |
| 65–74 | 7.5 | 3.4 | 0 | 5 | 7 | 10 | 22 |
| ≥75 | 21.9 | 8.3 | 4 | 16 | 20 | 26 | 65 |
| Meteorologic factors | | | | | | | |
| Mean temperature, °C | 23.6 | 4.9 | 8.2 | 19.6 | 24.8 | 27.8 | 31.8 |
| Max. temp, °C | 25.8 | 5.2 | 9.3 | 21.7 | 26.8 | 30.1 | 35.4 |
| Min. temp, °C | 21.7 | 5.0 | 6.4 | 17.9 | 23.1 | 25.9 | 29.4 |
| DTR, °C | 4.0 | 1.4 | 0.7 | 3.1 | 4.0 | 4.9 | 12.2 |
| In cool season | 3.9 | 1.5 | 0.7 | 2.9 | 3.9 | 4.9 | 12.2 |
| In warm season | 4.1 | 1.3 | 0.8 | 3.3 | 4.1 | 5 | 9.8 |
| Humidity, % | 78.3 | 9.8 | 31.0 | 74.0 | 79.0 | 85.0 | 98.0 |
| Air pollution concentrations, μg/m³ | | | | | | | |
| PM₁₀ | 53.6 | 27.6 | 14.0 | 31.5 | 47.9 | 70.2 | 196.0 |
| NO₂ | 57.8 | 20.6 | 14.9 | 43.2 | 55.6 | 69.0 | 168.2 |
| O₃ | 41.6 | 25.1 | 2.3 | 22.0 | 35.2 | 56.1 | 180.0 |
| SO₂ | 20.3 | 13.8 | 2.8 | 11.3 | 16.9 | 24.4 | 134.9 |
HF indicates heart failure; Pₓ, xth percentiles; Max., maximum; and Min., minimum.
women and elders were more vulnerable to the temperature change within a day.

### Discussion

Although the seasonal variation of HF hospitalizations\(^9,19\) or the association between cold temperature and HF morbidity\(^10,18\) has been well documented, the temperature change within a day or DTR is still a novel environmental risk factor that should be aware of by patients with HF and caretakers. In this time series study, we compared the day-to-day variations of DTR and the day-to-day variations of emergency HF hospitalizations and estimated the short-term effects of DTR on HF exacerbations. We found significantly adverse effects of DTR on HF admissions on the current day and lasting for the following several days. The effects of DTR were robust to the adjustment for daily absolute temperature (mean or minimum) and air pollution concentrations and were significantly greater in the cool season. Female and elderly subjects were the subgroups that were more sensitive to the DTR effects.

Seasonal variation of HF hospital admissions was obvious in Hong Kong (Figure 1), displaying a significant winter-peak, as previous studies have shown not only in the northern hemisphere,\(^4,19\) but also in the southern hemisphere.\(^9\) Physiological mechanisms underlying the association between the cold temperature and greater HF hospitalizations have been well documented.\(^18\) For example, the hemodynamic stresses and neurohumoral activation that accompany a reduction in temperature may exacerbate HF, induce myocardial ischemia, and precipitate arrhythmias. Furthermore, both ischemia and arrhythmias could further increase the risk of HF decompensation. Other mechanisms may relate to the pulmonary infection in seasonal variation. Respiratory infections are more frequent in winter and could precipitate HF. The short-term cold exposure in young healthy subjects could also initiate a mild inflammatory reaction and a tendency for an increased state of hypercoagulability.\(^35\)

Several previous studies have also found the adverse effects of temperature change within a day on cardiorespiratory morbidity\(^12,13\) and mortality.\(^14–16\) Plausible biological mechanisms of DTR on cardiovascular diseases have been hypothesized. Greater DTR may cause cardiovascular-related diseases by increasing blood pressure, oxygen uptake, heart rate, and cardiac workload.\(^12\) Keatinge et al\(^13\) found that increases in blood platelets, red cells, and viscosity were associated with normal thermoregulatory adjustments to temperature change. Bull\(^34\) argued that weather changes may affect either humoral or cellular immunity. Female or elderly subjects might have either lower thermoregulatory responses or weaker immunity so that they were more vulnerable to the temperature change within a day.

The impact of colder temperature on cardiovascular morbidity or mortality has been found not only in the regions with cold winter climate, but also in the regions with relatively warmer weather. Those single-location studies

### Table 2. Sensitivity Analyses for the Effects of DTR on Emergency HF Hospital Admissions by Lags (Lag_0–Lag_5 and Overall Cumulative)

<table>
<thead>
<tr>
<th>Lag Days</th>
<th>PM(_{10})</th>
<th>NO(_2)</th>
<th>O(_3)</th>
<th>SO(_2)</th>
<th>Effect Estimate(\alpha)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lag(_0)</td>
<td>0.87 (0.31 to 1.43)§</td>
<td>0.91 (0.36 to 1.47)§</td>
<td>0.41 (−0.16 to 0.97)</td>
<td>0.88 (0.32 to 1.44)§</td>
<td>0.57 (0.00 to 1.15) §</td>
</tr>
<tr>
<td>Lag(_1)</td>
<td>0.89 (0.34 to 1.43)§</td>
<td>0.82 (0.28 to 1.37)§</td>
<td>0.52 (−0.04 to 1.08)</td>
<td>0.78 (0.23 to 1.32)§</td>
<td>0.77 (0.20 to 1.34)§</td>
</tr>
<tr>
<td>Lag(_2)</td>
<td>0.81 (0.28 to 1.34)§</td>
<td>0.69 (0.16 to 1.22)§</td>
<td>0.46 (−0.09 to 1.00)</td>
<td>0.59 (0.06 to 1.12)§</td>
<td>0.79 (0.23 to 1.34)§</td>
</tr>
<tr>
<td>Lag(_3)</td>
<td>0.86 (0.35 to 1.38)§</td>
<td>0.69 (0.17 to 1.21)§</td>
<td>0.32 (−0.21 to 0.85)</td>
<td>0.62 (0.10 to 1.14)§</td>
<td>0.80 (0.26 to 1.35)§</td>
</tr>
<tr>
<td>Lag(_4)</td>
<td>0.63 (0.12 to 1.14)§</td>
<td>0.49 (−0.02 to 1.01)</td>
<td>0.26 (−0.27 to 0.79)</td>
<td>0.40 (−0.12 to 0.91)</td>
<td>0.69 (0.15 to 1.23)§</td>
</tr>
<tr>
<td>Lag(_5)</td>
<td>0.63 (0.12 to 1.14)§</td>
<td>0.50 (−0.01 to 1.02)</td>
<td>0.34 (−0.19 to 0.88)</td>
<td>0.51 (−0.01 to 1.03)</td>
<td>0.56 (0.02 to 1.10)§</td>
</tr>
<tr>
<td>Overall cumulative(\alpha)</td>
<td>3.76 (3.36 to 4.16)§</td>
<td>3.02 (2.63 to 3.42)§</td>
<td>2.33 (1.94 to 2.73)§</td>
<td>2.85 (2.45 to 3.25)§</td>
<td>3.39 (2.99 to 3.79)§</td>
</tr>
</tbody>
</table>

Values represent ERR% (95% CI) per 1°C increment of DTR. CI indicates confidence interval; DTR, diurnal temperature range; ERR, excess relative risk; HF, heart failure; NO\(_2\), nitrogen dioxide; O\(_3\), ozone; PM\(_{10}\), particles with an aerodynamic diameter <10 μm; and SO\(_2\), sulfur dioxide.

*Effects were estimated from core model (Equation 1).
†Effects were estimated by replacing the terms of mean temperature with the minimum temperature in core model (Equation 1).
‡Overall cumulative effects of DTR lasting for 0 to 5 days were estimated by distributed lag models.
§Statistically significant effect estimates.
conducted in warmer areas with higher long-term mean temperatures tended more frequently to report detrimental effects of cold and tended to report effect estimates of greater magnitude.\textsuperscript{10,35} Hong Kong has a moderate cool winter with mean temperature 19.5°C (range, 8.2°C–22.0°C) in cool season; residents may be more vulnerable to low temperature and daily temperature change. Furthermore, indoor heating system is uncommon in Hong Kong. Hence, a decrease in the outdoor temperature can affect indoor temperature rather quickly in winter and affect the patients at risk. In contrast, during the hot and humid summer in Hong Kong (temperatures of 25°C–30°C and humidity of 70%–90% between 10th and 90th percentiles), people usually use air-conditioning indoors and engage in less outdoor activities, thus reducing the risks of temperature change. This might be the reason that we did not find the association between the DTR and HF admissions in the warm season.

Our findings provide some insight into the prevention of temperature change–related emergency HF hospitalizations. Early warning system for impending large temperature change may reduce the impact of DTR on population health. Female and elderly subjects, especially the socially isolated and economically disadvantaged, should be monitored closely and offered access to heated indoor environments to reduce the great DTR exposure. They should be given advice on appropriate clothing when a rapid drop in temperature is predicted. Monitoring patients such as home telemonitoring during follow-up to detect deterioration in the hope of reversing it and preventing an adverse outcome was also suggested.\textsuperscript{1}

The strength of this study relied on the reliable and comprehensive hospital admission data, which were central-computerized source of patient data covering >90% of the population in Hong Kong. We included >100 thousands HF emergency admissions during the 8-year study period, which is the largest single-city study to estimate the association between DTR and HF hospitalization to date.

Some limitations should be noted. As in other time series studies, we used available outdoor monitoring data to represent the population exposure to ambient temperature, temperature change, and air pollution. Indoor temperature and personal exposure data were not available. Exposure misclassification should not be ignored because of the widely used air-conditioning in warm season. Another limitation was that we could not identify the readmissions for patients with HF according to the available data. We have to put the first onset of HF and the readmission patients together and observed the increase of DTR associated with the increase of the total hospital admissions for HF. A previous study demonstrated that in the 6 to 9 months after the initial HF admission, 60% of patients had ≥1 readmissions for any cause and HF accounted for 28% of all readmissions.\textsuperscript{36} Further study is needed to examine the association between DTR and the first onset or readmission of HF separately, which may help to identify specific target group(s) for focused prevention. Furthermore, studies in other settings with different climate and larger DTR are recommended to provide a better understanding of the effects of temperature change on health.

In conclusion, we found significantly short-term adverse effects of DTR on emergency HF admissions. The effects of DTR were significantly greater in the cool season. Women and elders were much more vulnerable to the temperature change. Policymakers and hospitals should take into account the increased demand of specific facilities for susceptible population in cool season with wider daily temperature variations.

Acknowledgments

We thank the Hospital Authority for providing hospital admissions data, the Hong Kong Observatory for providing temperature and humidity data, and the Hong Kong Environmental Protection Department for providing air pollution data.

Disclosures

None.

References


**CLINICAL PERSPECTIVE**

In this study, we hypothesized that greater temperature change within a day (ie, diurnal temperature range) might act as an additional stress to precipitate heart failure in persons with pre-existing heart diseases and hence could be identified as a risk factor for heart failure exacerbation. We conducted a time series study to examine the association between daily temperature change and emergency hospital admissions for heart failure, after adjusting for the time trend, seasonality, mean/minimum temperature, humidity, and levels of outdoor air pollution. We observed that the adverse effects of diurnal temperature range on emergency heart failure admissions on the same day and lasting for the following several days. Diurnal temperature range exhibited significantly greater effect in cool season. Women and elders were much more vulnerable to the daily temperature changes. Our findings suggest that on days with predicted wide daily temperature variations, especially during the cool season, women and elders may be advised to avoid exposures to the extreme temperatures (eg, by staying indoors and keeping the indoor temperature within a narrow comfortable range). However, clinicians and health service providers should get prepared for an upsurge of emergency hospital admissions for heart failure on those days.
Is Greater Temperature Change Within a Day Associated With Increased Emergency Hospital Admissions for Heart Failure?
Hong Qiu, Ignatius Tak-sun Yü, Lap Ah Tse, Linwei Tian, Xiaorong Wang, and Tze Wai Wong

Circ Heart Fail. 2013;6:930-935; originally published online August 9, 2013; doi: 10.1161/CIRCHEARTFAILURE.113.000360

Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3289. Online ISSN: 1941-3297

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