



# Physician connect

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you '**Physician connect**' which contains latest and interesting news in the field of Medicine.

This issue contains

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- Vericiguat and Heart Failure with Reduced Ejection Fraction: VICTORIA study
- Insomnia and Chronic Pain: A Swedish Longitudinal Population Study (SwePain)

Should you require any specific article or medical information, please feel free to contact us at

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Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

## Association of Non-dipper Heart Rate and Brain Natriuretic Peptide on CV Events: J-HOP Study

Many reports have shown that a blunted nocturnal drop in an individual's blood pressure (BP) (i.e., the non-dipper BP pattern) is related to cardiovascular (CV) events. Like BP, the heart rate (HR) also undergoes diurnal variation in response to changes in sympathetic nerve activity. Specifically, the HR decreases with increases in parasympathetic activity.

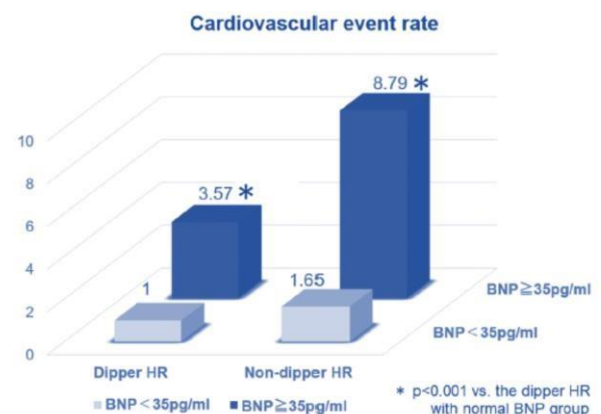
It has also been reported that brain natriuretic peptide (BNP) is associated with CV events, and we showed that the non-dipper HR status was related to a high level of BNP. However, the relationships among the non-dipper HR pattern, BNP levels, and CV prognoses have not been clarified. This study evaluated the association between CV events, non-dipper HR status, and BNP levels in high-risk Japanese outpatients from the Japan Morning Surge-Home Blood Pressure (J-HOP) study.

**The combination of non-dipper HR and higher BNP was associated with a higher incidence of CV events.**

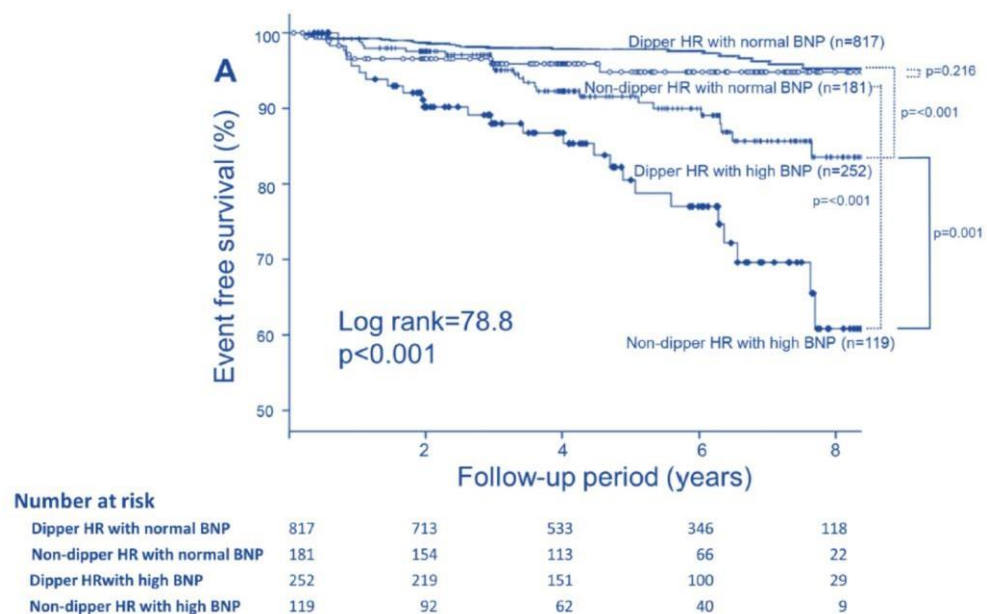
A subgroup of 1,369 patients from the study were evaluated; these were patients who had CV risk factors and had undergone ambulatory blood pressure (BP) monitoring.

HR non-dipping status was defined as  $(\text{awake HR} - \text{sleep HR})/\text{awake HR} < 0.1$ , and high BNP was defined as  $\geq 35$  pg/ml. We divided the patients into four groups according to their HR dipper status (dipping or nondipping) and BNP level (normal or high).

The mean follow-up period was  $60 \pm 30$  months. The primary endpoints were fatal/nonfatal CV events (myocardial infarction, angina pectoris, stroke, hospitalization for heart failure, and aortic dissection). The CV event rates are depicted in the figure.



The patients with non-dipper HR and high BNP had a higher incidence of CV events than the patients in the other three groups combined (log rank = 78.8,  $P < 0.001$ ; Figure).



During the follow-up period, 23 patients (2.8%) in the dipper HR with normal BNP group, 8 patients (4.4%) in the non-dipper HR with normal BNP group, 24 patients (9.5%) in the dipper HR with high-BNP group, and 25 patients (21.0%) in the non-dipper HR with high-BNP group suffered primary endpoints (log rank 78.8,  $P < 0.001$ ). Non-dipper HR was revealed as an independent predictor of CV events (hazard ratio, 2.13; 95% confidence interval, 1.35–3.36;  $P = 0.001$ ) after adjusting for age, gender and smoking, dyslipidemia, diabetes mellitus, chronic kidney disease, BNP, non-dipper BP, 24-h HR, and 24-h systolic blood pressure.

In this study, the non-dipper HR pattern was associated with a high incidence of CV events, but only among the patients with high-BNP levels. Thus a high-BNP level and the non-dipper HR status might be useful for the risk stratification of CV events.

Source: Ogoyama Y et al. Am J Hypertens. 2020;33(5):430-438. doi:10.1093/ajh/hpaa025

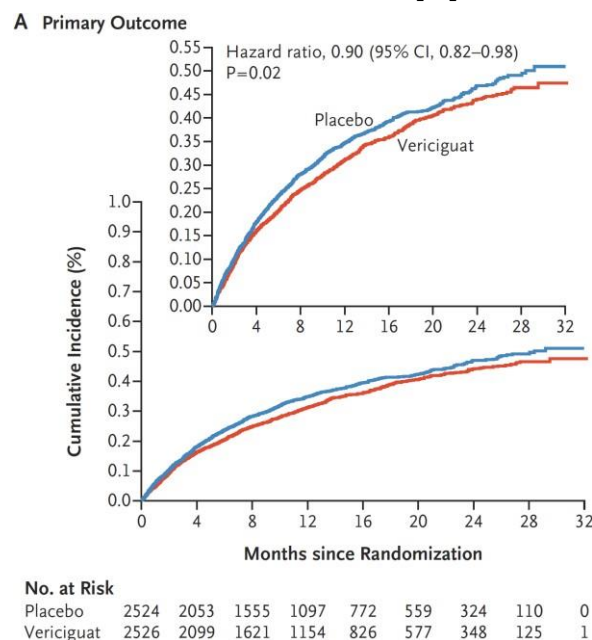
## Vericiguat and Heart Failure with Reduced Ejection Fraction: VICTORIA study

The effect of vericiguat, a novel oral soluble guanylate cyclase stimulator, in patients with heart failure and reduced ejection fraction who had recently been hospitalized or had received intravenous diuretic therapy is unclear.

In this phase 3, randomized, double-blind, placebo-controlled trial, we assigned 5050 patients with chronic heart failure (New York Heart Association class II, III, or IV) and an ejection fraction of less than 45% to receive vericiguat (target dose, 10 mg once daily) or placebo, in addition to guideline-based medical therapy. The primary outcome was a composite of death from cardiovascular causes or first hospitalization for heart failure.

**The incidence of death from cardiovascular causes or hospitalization for heart failure was lower among those who received vericiguat.**

Over a median of 10.8 months, a primary-outcome event occurred in 897 of 2526 patients (35.5%) in the vericiguat group and in 972 of 2524 patients (38.5%) in the placebo group (hazard ratio, 0.90; 95% confidence interval [CI], 0.82 to 0.98;  $P=0.02$ ). A total of 691 patients (27.4%) in the vericiguat group and 747 patients (29.6%) in the placebo group were hospitalized for heart failure (hazard ratio, 0.90; 95% CI, 0.81 to 1.00). Death from cardiovascular causes occurred in 414 patients (16.4%) in the vericiguat group and in 441 patients (17.5%) in the placebo group (hazard ratio, 0.93; 95% CI, 0.81 to 1.06). The composite of death from any cause or hospitalization for heart failure occurred in 957 patients (37.9%) in the



vericiguat group and in 1032 patients (40.9%) in the placebo group (hazard ratio, 0.90; 95% CI, 0.83 to 0.98;  $P=0.02$ ). Symptomatic hypotension occurred in 9.1% of the patients in the vericiguat group and in 7.9% of the patients in the placebo group ( $P=0.12$ ), and syncope occurred in 4.0% of the patients in the vericiguat group and in 3.5% of the patients in the placebo group ( $P=0.30$ ).

Among patients with high-risk heart failure, the incidence of death from cardiovascular causes or hospitalization for heart failure was lower among those who received vericiguat than among those who received placebo.

Source: Armstrong PW et al. N Engl J Med 2020; 382:1883-1893. DOI: 10.1056/NEJMoa1915928

## Insomnia and Chronic Pain: A Swedish Longitudinal Population Study (SwePain)

Chronic pain is a very common condition and affects significant number of population across the globe. However, based on the spatial distribution of pain on the body, chronic pain constitutes a spectrum from local pain (e.g. lowback pain) to generalised or widespread pain (e.g. fibromyalgia).

Recent evidence suggests that insomnia negatively influences the occurrence of generalized pain. This study examined whether insomnia is a risk factor for the transition from

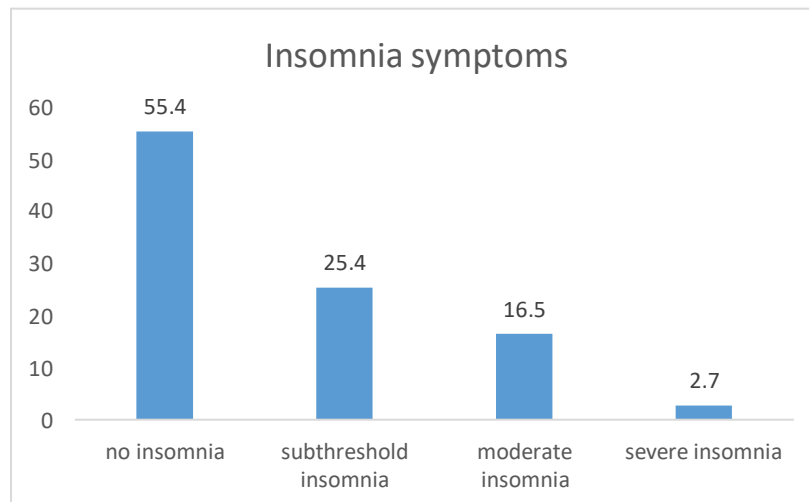
**There is a strong prospective relationship between insomnia symptoms and the transition from relatively localized to generalized pain.**

local pain to generalized pain (i.e., spreading of pain).

This longitudinal study, with a follow-up of 24 months, included 959 participants (mean age: 55.8 years; SD: 13.9) with local or regional pain at baseline. Participants were grouped by insomnia symptoms as measured by the Insomnia Severity Index. Spreading of pain was measured by body manikins based on the spatial distribution of pain on the body. We defined two outcome categories; one with relatively localized pain (i.e., local pain and moderate regional pain), and one with relatively generalized pain (i.e., substantial regional pain and widespread pain). Baseline age, sex, education, depressive symptoms, anxiety symptoms,

catastrophizing, pain intensity, and spread of pain were also included in the Generalized Linear Model analysis.

The unadjusted model showed that the risk of spreading of pain increased with an increase in insomnia symptoms (no insomnia: 55.4%; subthreshold insomnia: 25.4% moderate insomnia: 16.5% and severe insomnia: 2.7%).



The risk increased in a dose-dependent manner; moderate insomnia risk ratio (RR) 2.34 (95% confidence interval [CI]: 1.34 – 4.09) and severe insomnia RR 4.13 (95% CI: 1.56 – 10.92). The results were maintained in the fully adjusted model although moderate regional pain was the strongest predictor RR 6.95 (95% CI: 3.11-15.54).

Source: Wiklund T et al. Eur J Pain. 2020;10.1002/ejp.1582. doi:10.1002/ ejp. 1582 [published online ahead of print].



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