

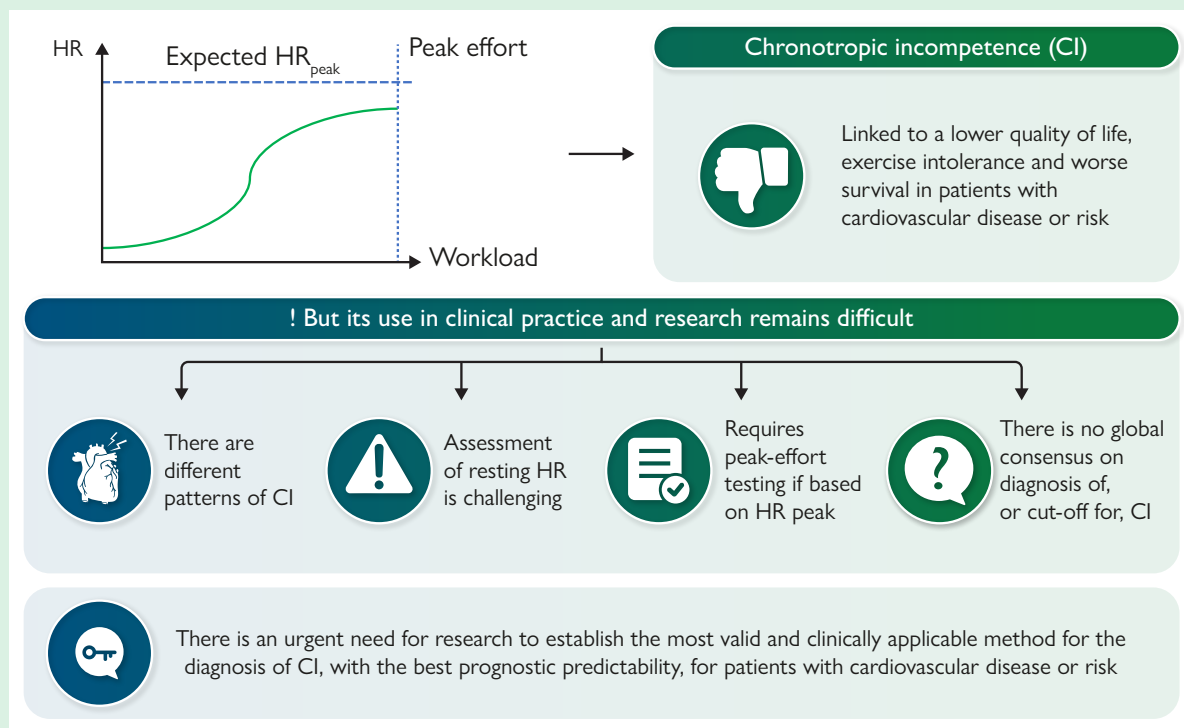
# Chronotropic incompetence in cardiovascular disease: a call for the establishment of a standardized and valid detection method

Dominique Hansen <sup>1\*</sup>

<sup>1</sup>REVAL/BIOMED (Rehabilitation Research Centre), Hasselt University, Wetenschapspark 7, Diepenbeek 3590, Belgium

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## Graphical Abstract



This editorial refers to 'Diagnosing chronotropic incompetence: a scoping review of current approaches and their application in a cardiac rehabilitation cohort', by M. Vermeiren *et al.* <https://doi.org/10.1093/eurjpc/zwag253>.

Chronotropic incompetence (CI), defined as the inability of the heart to appropriately increase its rate (heart rate, HR) in

response to exercise, can be highly common in patients with cardiovascular disease (CVD) or risk, even in those without taking beta-blockers. CI can be caused by abnormalities in the vagal and sympathetic outflow to the sinus node, baroreflex, metaboreflex or mechanoreflex abnormalities, impaired exercise-induced catecholamine release, sinus node dysfunction, or the combination thereof: its aetiology can thus be very complex.<sup>1</sup> In obesity

(even already in children/adolescents),<sup>2</sup> type 2 diabetes,<sup>1</sup> heart failure,<sup>3</sup> chronic coronary syndrome<sup>4</sup> and sinus node disease this anomaly can often be encountered during exercise testing. Such observation should however not be ignored: CI is independently related to reductions in exercise capacity and quality of life, as well as a worse prognosis (e.g. increased risk for hospitalization or premature death).<sup>5</sup> Moreover, the chronotropic response to exercise can be improved by the participation in an exercise intervention in some patients with CVD, and, thus, can be remediated to some extent.<sup>6</sup>

However, the main limitation is current clinical practice and scientific research is how or when to diagnose CI exactly: plenty of different criteria or approaches have been described. This leads to wide prevalence ranges of CI among patients with CVD (risk) in previous reports<sup>7</sup> and it remains open which of those are valid, reliable and truly predictable. Hence, this issue should finally be settled, so that clinicians can rely on valid methods to diagnose CI, adjust medical treatment accordingly, and that in scientific research projects the aetiology, prevalence, and consequences of CI can be studied in a correct manner.

Recently, Vermeiren *et al.*<sup>8</sup> went into greater detail on this highly relevant topic. They ( i ) conducted a scoping review to provide a comprehensive overview of available methods to define CI, and ( ii ) performed a retrospective cohort study to illustrate how different diagnostic approaches affect the classification of CI in patients ( $n = 2869$ ) enrolled in a cardiac rehabilitation program by quantifying the agreement between methods in clinical practice.

In this article,<sup>8</sup> the authors give a nicely detailed overview of the methods to determine CI, with ranking, advantages and disadvantages. From 45 studies, 17 different methods to establish CI have been described, which can be categorized into ( i ) the HR in relation to workload, exercise time or oxygen uptake or ( ii ) achieving a specific HR threshold. Of those 45 studies, only eight investigated patients with CVD. A complicating factor in the diagnosis of CI is how this phenomenon clinically emerges: there are different potential patterns. There could be a failure to reach the predicted peak HR ( $HR_{peak}$ ), a delayed attainment of  $HR_{peak}$ , an inadequate submaximal or recovery HR response, or HR instability. Hence, by only looking at  $HR_{peak}$ , as often done in clinical practice, this is not taken into account. Also a correct assessment of the resting HR, reaching true maximal effort during exercise testing, and (the individually different response to) beta-blocker therapy can be challenging in the determination of CI. Nevertheless, the authors firmly conclude that methods which rely on an age-predicted  $HR_{peak}$  for the calculation of the chronotropic response (e.g.  $220 - \text{age}$ ) are overly inaccurate, and should thus not be used. When the different methods for the detection of CI were applied in their cohort, the prevalence of CI varied widely (6.2–72.4%), and the agreement between definitions was poor.

Taking all these observations together (see central illustration), the authors conclude that a definition based on the evolution of the HR relative to the metabolic demand should

preferentially be developed, independent of  $HR_{peak}$  prediction models, CPET maximality, or the patient's physical fitness. Moreover, the CI detection method should provide a continuous measure, which can be compared with reference percentiles from a healthy population, adjusted for relevant clinical variables (e.g. age, sex, and body composition, cardiorespiratory fitness), or plotted against prognostic outcomes (e.g. survival, hospitalization).

Hence, more research effort on this topic is urgently warranted: this can potentially lead to an optimal and universally agreed method to establish CI and thus a better prediction of prognosis in patients with CVD (risk) and a better understanding of the pathophysiology of CVD.

## Author contributions

Dominique Hansen (Conceptualization, Writing—original draft, Writing—review & editing [lead])

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None.

**Conflict of interest:** None declared.

## Data availability

Not of relevance in this paper (no data used).

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