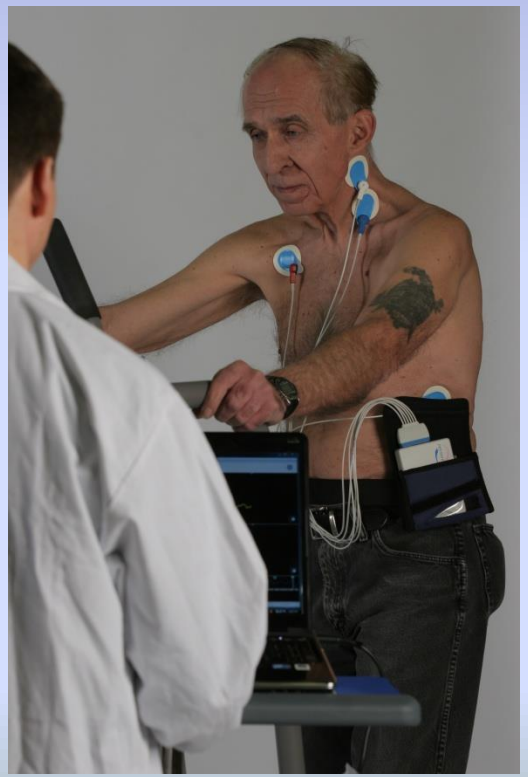
Can noninvasive cardiac hemodynamics during exercise be of help to understand and predict responses to exercise training in patients with cardiac disease?



Frank Bour, Ph. D, University of Paris,
CEO PhysioFlow
Taiwan, April 2026

Agenda for the Presentation

- Context, challenges in Cardiac Rehabilitation (CR)
- Previous studies involving non invasive exercise haemodynamics in CR
- The SM-ICG contractility index (CTi) during exercise
- Studies 1: CTi profiles and prediction of cardiac rehabilitation outcomes in the general cardiovascular patients
- Studies 2: CTi profiles and prediction of cardiac rehabilitation outcomes in heart failure patients
- Conclusion and perspective

Context

- Cardiac Rehabilitation (CR) significantly increases exercise capacity and reduces one year mortality in all types of cardiac patients (- 28% CAD and -18% in HF), and also rehospitalization rate (-18% in CAD and -20-30% in HF) (French statistics)

- There are still up to 1/3 of non responders reported in the literature
- Lack of response to exercise training is clearly associated with a worsening of prognosis and have negative psychological effect in patients
- The reasons for non response have been studied but there is no consensus
- Also, there is no clearly defined criteria for predicting the response to CR

Previous Studies Involving PhysioFlow in CR

- Compared to moderate intensity interval exercise, optimized high intensity interval exercise elicited a greater central hemodynamic response in patients with CHF (Gayda M, Normandin E, Meyer P, Juneau M, Haykowsky M, Nigam A. Central hemodynamic responses during acute high-intensity interval exercise and moderate continuous exercise in patients with heart failure. Appl Physiol Nutr Metab. 2012 Dec;37(6):1171-8.)

- The analysis of the response to training in patients with HFrEF according to the different steps of oxygen transport revealed different phenotypes on VO2peak responses, namely responses in either oxygen convection and/or diffusion. (Legendre A, Moatemri F, Kovalska O, Balice-Pasquinelli M, Blanchard JC, Lamar-Tanguy A, Ledru F, Cristofini P, Iliou MC. Responses to exercise training in patients with heart failure. Analysis by oxygen transport steps. Int J Cardiol. 2021 May 1;330:120-127)

- Responders showed improvements in peak hemodynamic parameters. These results pave the way for other studies to determine how the individualization of exercise training programs and peak hemodynamic parameters potentially linked to a better positive response status (in HFrEF). (Kirsch M, Iliou MC, Vitiello D. Hemodynamic Response to Exercise Training in Heart Failure With Reduced Ejection Fraction Patients. Cardiol Res. 2024 Feb;15(1):18-28.)

Previous Studies Involving PhysioFlow in CR

- Peripheral and ventilatory responses more than central adaptations could be responsible for the ˙VO2peak change with ECR in CHD patients. (Girault A, Leprêtre PM, Trachsel LD, Besnier F, Boidin M, Lalongé J, Juneau M, Bherer L, Nigam A, Gayda M. Determinants of V̇+O2peak Changes After Aerobic Training in Coronary Heart Disease Patients. Int J Sports Med. 2024 Jun;45(7):532-542.)

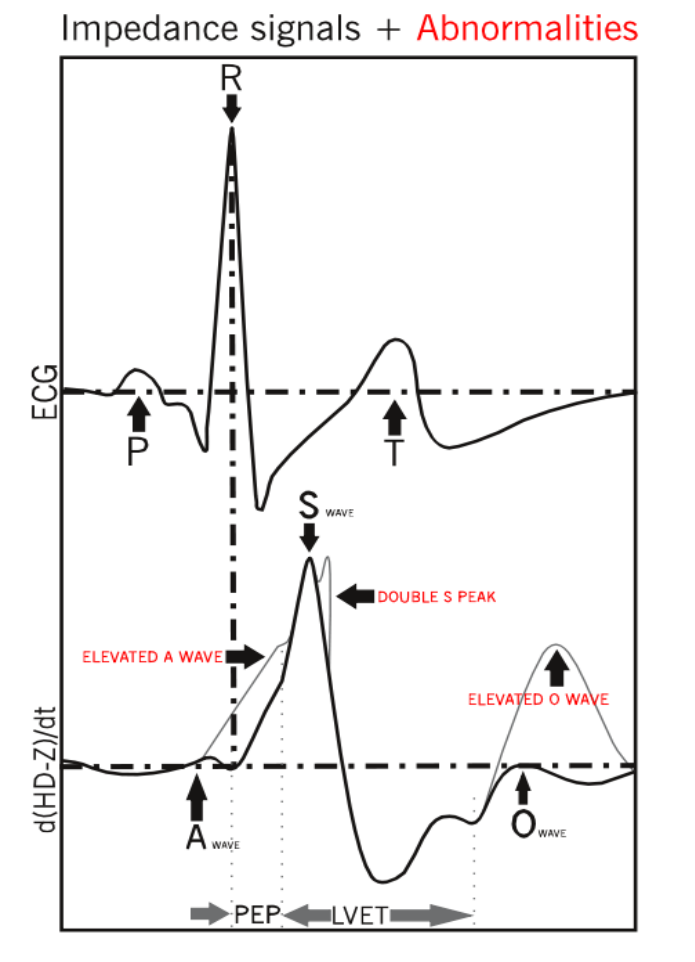
- Among CHD patients, the responder group showed a better improvement in peak cardiac output via an increase in peak stroke volume and heart rate and a reduced systemic vascular resistance than the NonResponder group (Kirsch M, Vitiello D, Trachsel LD, Boidin M, Lalongé J, Juneau M, Bherer L, Nigam A, Gayda M. Cardiac hemodynamics phenotypes and individual responses to training in coronary heart disease patients. Scand J Med Sci Sports. 2024 Apr;34(4):e14633.)

These research studies pave the way for the introduction of routine evaluation of noninvasive exercise hemodynamics in CR

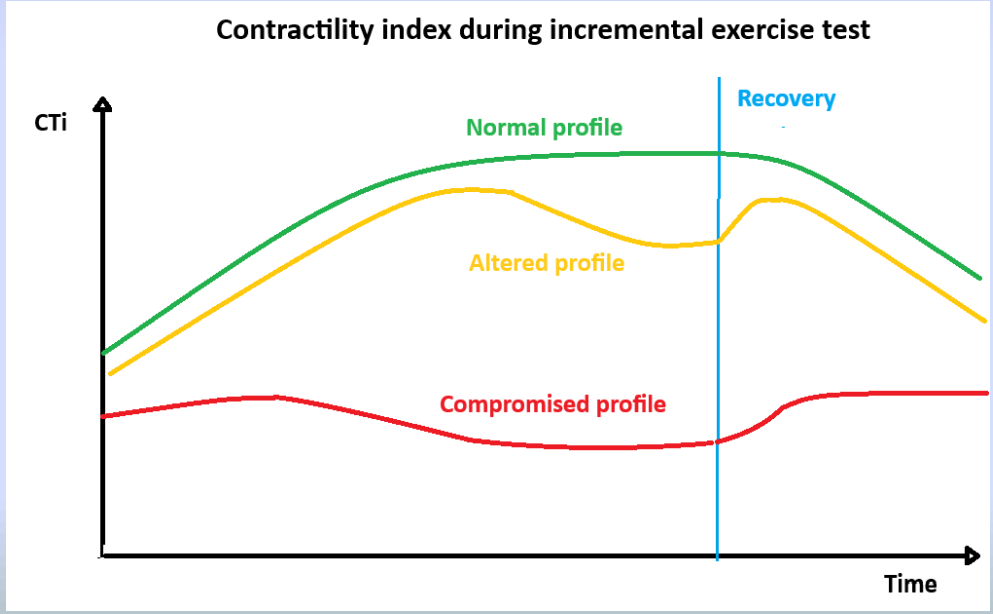
They need to be expanded and refocused on a more powerful and easy to measure determinant of cardiac output, the left ventricular contractility

New Perspective : Analysis of Contractility

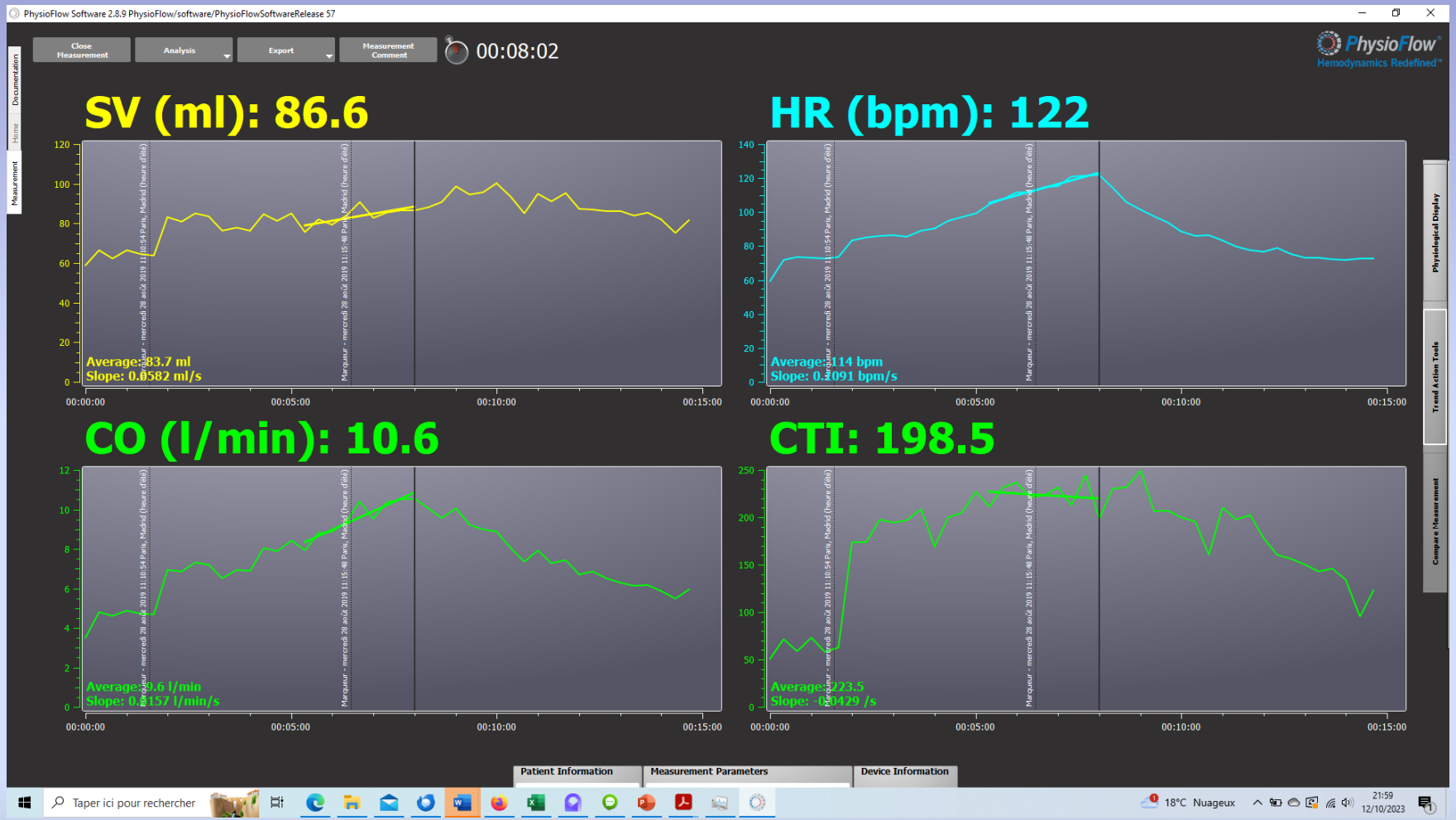
CTi (Contractility index) is understood as the peak ejectional flow velocity (S-wave or $d(HD\text{-}Z)/dt_{max}$)



3 main profiles during exercise tests (incremental, cyclo ergometer)

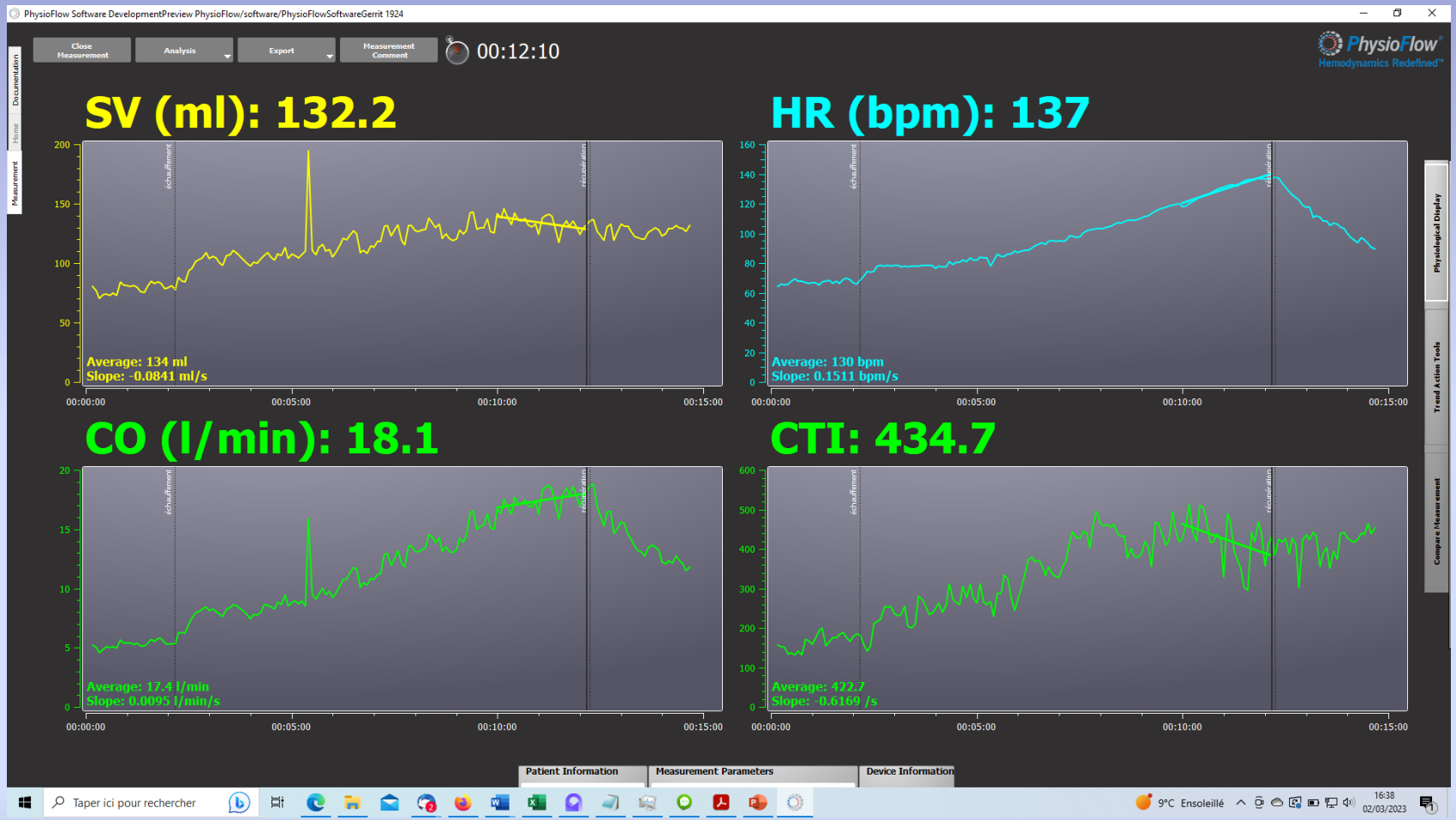


Analysis of Contractility Index: Real measurements



CTi goes into plateau during exercise (normal profile)

Analysis of Contractility Index
Real measurements



CTi slope change before recovery (altered profile)

Analysis of Contractility Index
Real measurements

CTi collapses at the onset of exercise (compromised profile)

Promising Benefits of CTi:

- Easy to measure, not operator dependent
- Sensitive and reproducible, taken directly from heart impedance waveforms
- A more direct reflection of cardiac function than VO2 derived cardiac parameters (CTI equivalent of dV/dt)

Goal of the New Studies:

1) To compare the effects of Exercise Training (ET) in terms of VO_{2peak} response in cardiac patients according to the contractility profile (CTi) of their LV during the baseline exercise test (BasET).

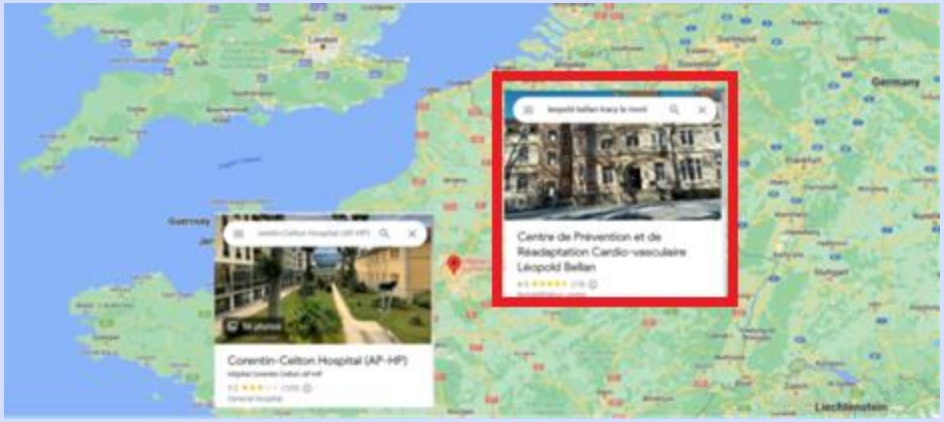
2) To determine if the changes in exercise contractility with training are correlated to the response to ET

Two French CR Centers

1) Studies (all types of CR patients), performed at the Leopold Bellan Cardiac Rehabilitation Centre (80 kms north of Paris)

1.1 **Signal-morphology impedance cardiography is a non-invasive tool for predicting responses to exercise-based cardiac rehabilitation**. (Bour F, Milstein E, Poty A, Garaud Y, Vitiello D, Leprêtre PM. Int J Cardiol. 2025 Jan 15;419:132670).

1.2 **Signal morphology impedance cardiography is a tool to explain the response of cardiac patients to cardiac rehabilitation in the presence of altered myocardial contractility profiles**. (Bour, F, Milstein Evan, Leprêtre Pierre-Marie. European Journal of Preventive Cardiology 2025/05/19, 10.1093)



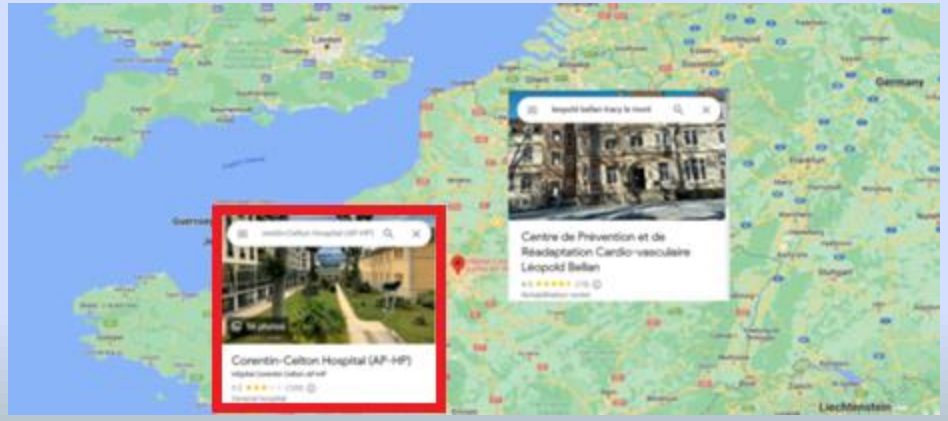
FONDATION LÉOPOLD BELLAN

Two French CR Centers

2) CR studies focused on heart failure patients, performed at the Corentin Celton Cardiac Rehabilitation Centre (Paris area)

2.1 **Signal-morphology impedance cardiography is a non-invasive tool to predict responses to exercise based cardiac rehabilitation in chronic heart failure patients** (F Bour, M C Iliou, D Vitiello, P M Lepretre, *European Heart Journal*, Volume 45, Issue Supplement_1, October 2024, ehae666.2975)

2.2 **Signal Morphology Impedance Cardiography Is A Non-invasive Tool To Better Understand The Response Or Lack Of Response To Exercise-based Cardiac Rehabilitation In Chronic Heart Failure**. (Frank Bour, Damien Vitiello, Marie Christine Iliou, Evan Milstein; Pierre Marie Lepretre, Accepted at the AACVPR 2025 annual meeting)

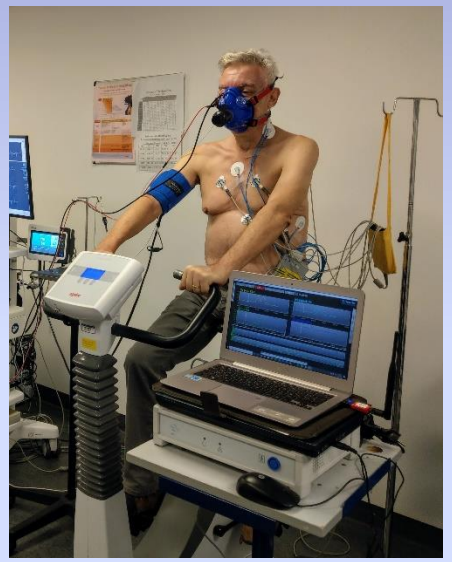


Hôpital Corentin-Celton AP-HP
ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Study 1.1 – CTI profiles and Prediction of Response to CR

- One of the expected effects of exercise training (ET) is to improve peak oxygen consumption (VO2peak) in patients with cardio-circulatory diseases.

- **Hypothesis:** The continuously monitored contractility response profile (CTi) of the left ventricle during the baseline exercise test (BasET) could be a good predictor of the VO2peak response to ET.



Introduction

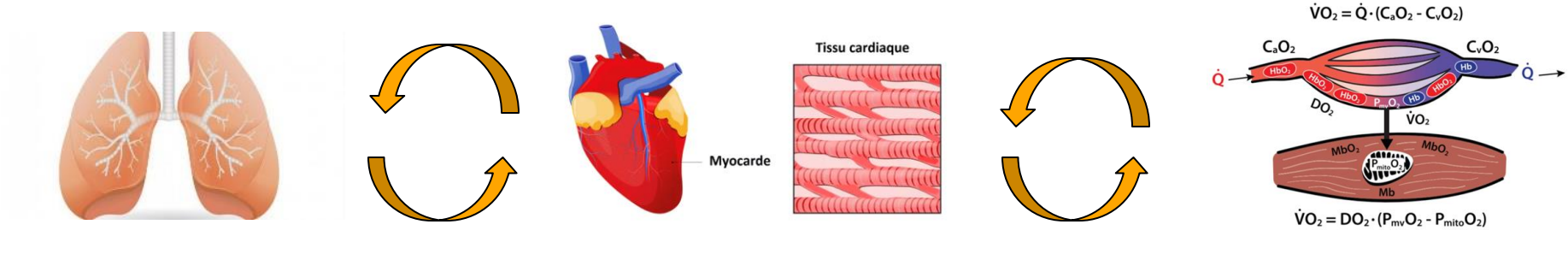
ΔVO_2 peak :

- variation in peak oxygen consumption after exercise training (ET) *(Witvrouwen et al. 2019)*

-> indirect reflection of changes in vital prognosis of patients with heart disease (HD) *(De Schutter et al. 2018)*

-> response from the 3 links in the transport chain of oxygen in the body *(Weatherwax et al. 2019, Legendre et al. 2021)*

BUT: with little or no relationship to initial cardiorespiratory responses (LVEF, VO_2 peak, HRmax, MaxW)



Patients and Methods

- 56 CV patients included, including 34 with coronary artery disease and 5 with heart failure
- 4 weeks ET, in line with French recommendations
- On average, the entire group increased their VO2peak (+13.57%, SD 22.94%)
- 41 patients out of 58 (70%) were considered responders $\Delta VO_2peak > 5\ \%$

CTi (Physioflow Lab1, Manatec, Poissy, France)

VO_2 (Quark b^2 , Cosmed, Rome, Italy)

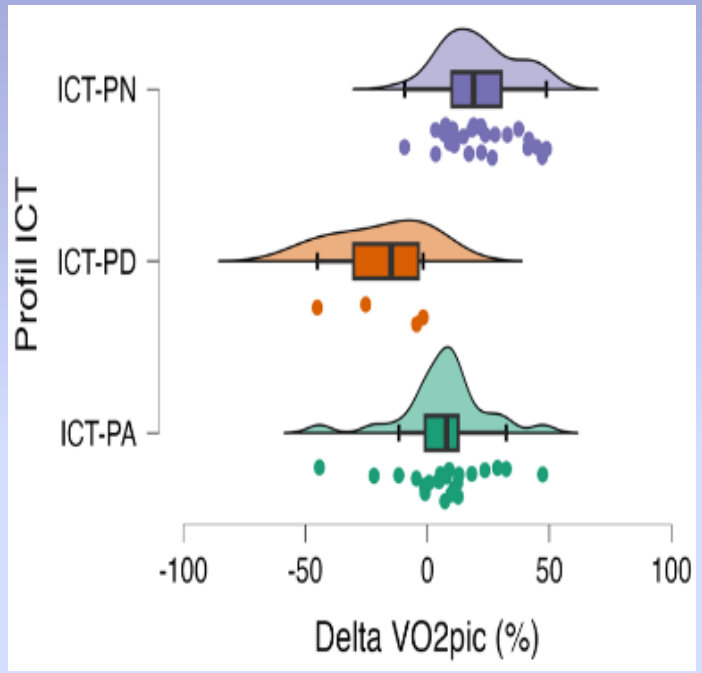
Results

normal CTi profile ΔVO_2 peak : 21.1±15.1%*
(VO_2 peak: 20.1±5.2mL.min^{-1} .kg^{-1} , n=27)

compromised CTi profile ΔVO_2 peak : -19.1±20.3%*
(VO_2 peak: 22.2±5.8 mL.min^{-1} .kg^{-1} , n=4)

altered CTi profile ΔVO_2 peak : 7.0±17.6%*
(VO_2 peak: 22.8±8.1 mL.min^{-1} .kg^{-1} , n=25)

* Significant difference between groups (p<0.05)



Patients with a normal CTi profile were 8.7 times more likely to respond positively to CR than those in the other groups combined (p = 0.012) (Logistic regression)

Conclusion :

* The contractile response of the left ventricle measured by SM-ICG during BasET seems to have an excellent predictive value for the response of cardiac patients to exercise-based cardiac rehabilitation

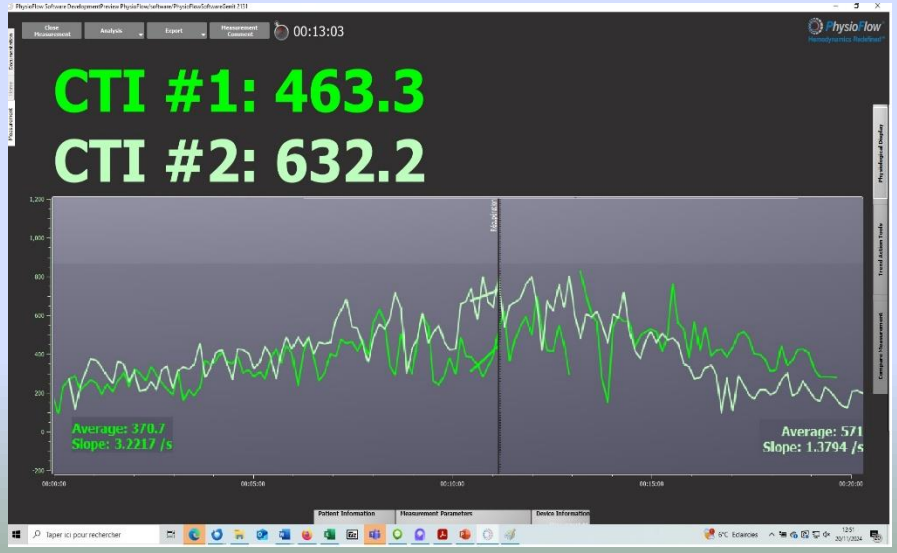
* However the patient group was not homogeneous, and there was a minority of HF patients

Study 1.2 – Abnomal CTI profiles and Mechanism of Response to CR

- Same patients, protocols, and methods as previous study

- **Results :** Among the patients with abnormal CTi profiles, the responders were able to improve their RestCTi to PeakCTi difference (expressed as percentage increase of the CTi from the resting phase before exercise started, to its highest value during the test) much more compared to the non-responders (pre-post EXCBR variation of 70.22± 55.38% vs. -12.03±24.92%, p=0.007).

- **Conclusion** : improving the contractility index response to exercise plays a significant role in improving overall fitness through cardiac rehabilitation in patients with impaired exercise contractility profiles



Study 2.1 - Presentation

* 74 cardiac rehab patients were included in this study performed at the Corentin Celton Centre (Paris area, France)

* All patients suffered from heart failure symptoms (and only 2 had LVEF above 40%)

* All underwent a full cardiopulmonary test upon admission (CPET + PhysioFlow exercise hemodynamics), + rest cardiac ultrasound.

* The training protocol include 5 session/week, combining endurance (interval training 3/week and moderate continuous training 2/week) and resistance (2-3 sessions/week), following French national recommendations

Analysis

- Average response on the patient group : **ΔVO2Peak : + 11.4 +/- 30,3%** (Median 10.9 %)

- **Responders ΔVO2Peak > +6%:** 2/3 of patients

CTi Profile	N=74
Normal	36
Altered	14
Compromised	24

Analysis - Logistic Regression

Response > 6 %					Wald Test		
	Estimate	Stand Error	Odds Ratio	z	Wald Statistic	df	p
(Intercept)	10.783	4.462	48176.200	2.417	5.840	1	0.016
Baseline VO_2/kg peak	0.026	0.107	1.026	0.240	0.058	1	0.810
HR 105	-0.039	0.018	0.961	-2.140	4.581	1	0.032
Age	-0.084	0.036	0.920	-2.345	5.501	1	0.019
CTI profile (D)	1.207	0.875	3.343	1.380	1.904	1	0.168
CTI profile (N)	1.954	0.806	7.057	2.424	5.877	1	0.015
BMI	-0.106	0.065	0.900	-1.629	2.652	1	0.103

Performance metrics : AUC 0.78, Sensitivity 0.87, Specificity 0.35

Study 2.1 - Conclusion

- The contractile response (CTi profile) of the left ventricle measured by SM-ICG during BasET seems to have a good predictive value for the response of CHF patients to cardiac rehabilitation

- These results can probably be enhanced by analyzing a combination of more parameters together (CTi profile and LVEF for instance)

Study 2.2 – Abnomal CTI profiles and Mechanism of Response to CR

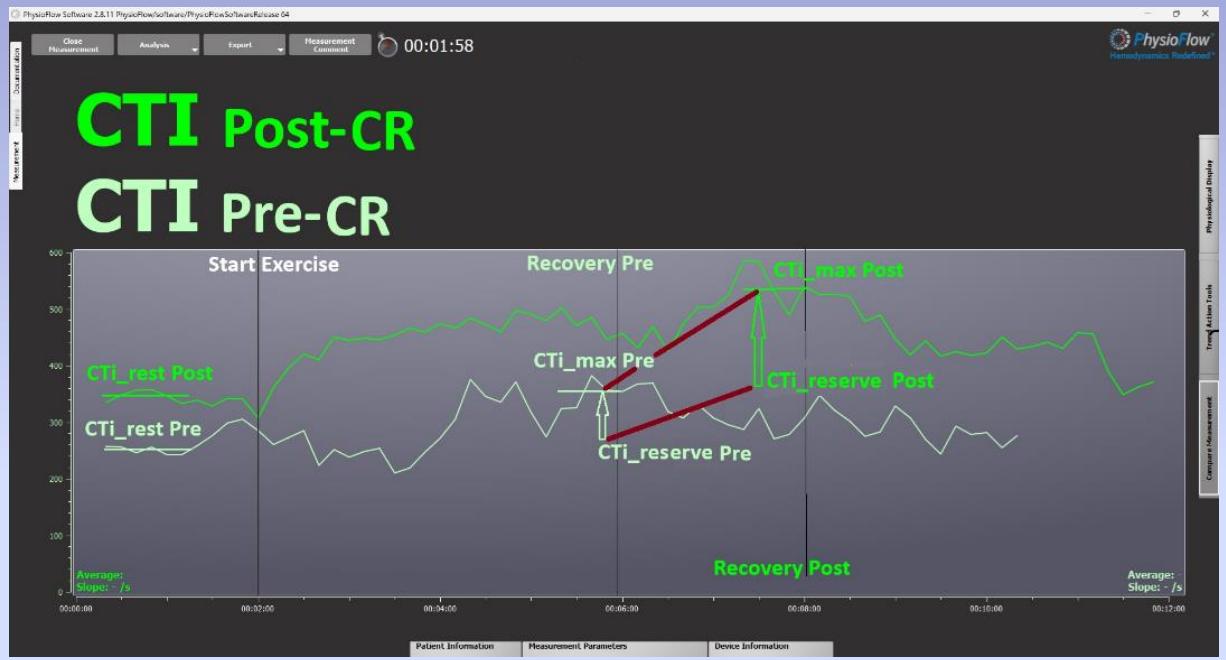
- Same patients (CHF), protocols, and methods as previous study. Patients were classified as responders if they achieved a ≥3.5 ml/kg/min increase in VO2peak (equivalent to +1 MET) or ≥24 W increase in maximal power output

- **Results :**

➢ Responders (n=32) showed a significant improvement in the contractility index (CTi) value at peak exercise (ΔCTimax: +64.3±78.2 vs −13.2±52.7, $p<0.001$) and in the reserve from rest to peak (ΔCTimax-rest: +49.9±54.3 vs −35.2±44.1 $p<0.001$), compared to non-responders (n=41).

➢ 94%of responders improved their ΔCTimax-rest, 93% of non-responders saw it decreased. No other baseline, demographic, echocardiographic, or laboratory parameter was highly predictive of, or correlated to, the response to CR.

Study 2.2 – Abnomal CTI profiles and Mechanism of Response to CR



Conclusion : Changes in CTi during exercise reflect myocardial contractile reserve, a sensitive marker of training response.

Practical Perspective

- Practical benefits in Cardiac Rehabilitation:
  - Better detection of potential non responders
  - Hemodynamic response is an independent marker of the response to CR (improved cardiac function)
  - The Future: New individualized training protocols ?

"Changes in VO2peak with training suggested a greater effect of MICE based on pSVmax compared to MICE based on VT1". (PM Lepretre, A Poty, T Porcher, F Hermel, A L Germain, F Krim, A L Gugenheim, Y Garaud, P6061 Changes in exercise capactiy of frailest patients with heart failure treated with standard exercise recommandations versus stroke volume response to exercise: a pilot study, *European Heart Journal*, Volume 39, Issue suppl_1, August 2018)

Healthcare Perspective

- This new approach may limit the number of non responders, improving outcomes and reducing costs

- Therefore, it may also improve patient participation (approx. 25% in France) + compliance with lifestyle changes