International Journal of Cardiology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Development of a clinical applicable graphical user interface to automatically detect exercise oscillatory ventilation: The VOdEX-tool☆,☆☆

Justien Cornelis [a,*,1], Tim Denis [a,b,1], Paul Beckers [a,c,d,1], Christiaan Vrints [c,d,1], Dirk Vissers [a,1], Maggy Goossens [b,1]

[a] University of Antwerp (Faculty of Medicine and Health Sciences), Department of Rehabilitation Sciences and Physiotherapy, Universiteitsplein 1, CDE S0.22, B-2610 Wilrijk, Belgium
[b] University of Antwerp (Faculty of Applied Engineering), Constrained Systems Lab (CoSys-Lab), Prinsstraat 13, B-2000 Antwerp, Belgium
[c] Antwerp University Hospital (Department of Cardiology), Wilrijkstraat 10, B-2650 Edegem, Belgium
[d] University of Antwerp (Faculty of Medicine and Health Sciences), Department of Medicine, Universiteitsplein 1, B-2610 Wilrijk, Belgium

ARTICLE INFO

Article history:
Received 7 September 2016
Received in revised form 14 November 2016
Accepted 18 December 2016
Available online xxxx

Keywords:
Exercise
Heart failure
Oscillatory ventilation
Wavelet analysis

ABSTRACT

Background: Cardiopulmonary exercise testing (CPET) gained importance in the prognostic assessment of especially patients with heart failure (HF). A meaningful prognostic parameter for early mortality in HF is exercise oscillatory ventilation (EOV). This abnormal respiratory pattern is recognized by hypo- and hyperventilation during CPET. Up until now, assessment of EOV is mainly done upon visual agreement or manual calculation. The purpose of this research was to automate the interpretation of EOV so this prognostic parameter could be readily investigated during CPET.
Methods and results: Preliminary, four definitions describing the original characteristics of EOV, were selected and integrated in the "Ventilatory Oscillations during Exercise-tool" (VOdEX-tool), a graphical user interface that allows automate calculation of EOV. A Discrete Meyer Level 2 wavelet transformation appeared to be the optimal filter to apply on the collected breath-by-breath minute ventilation CPET data. Divers aspects of the definitions i.e. cycle length, amplitude, regularity and total duration of EOV were combined and calculated. The oscillations meeting the criteria were visualised. Filter methods and cut-off criteria were made adjustable for clinical application and research. The VOdEX-tool was connected to a database.
Conclusions: The VOdEX-tool provides the possibility to calculate EOV automatically and to present the clinician an overview of the presence of EOV at a glance. The computerized analysis of EOV can be made readily available in clinical practice by integrating the tool in the manufactures existing CPET software. The VOdEX-tool enhances assessment of EOV and therefore contributes to the estimation of prognosis in especially patients with HF.
© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Heart failure (HF) is defined as a complex clinical syndrome resulting from any structural or functional impairment in ventricular filling or ejection of blood [1]. In developed countries, HF has a high prevalence (1–2%) and is a significant cause of death [2,3]. Researchers became aware of the importance of an early prognostic assessment in HF based on parameters derived from a cardiopulmonary exercise test (CPET) [4]. Recently, an oscillatory pattern in minute ventilation (VE) (l/min) during exercise, known as exercise oscillatory ventilation (EOV), has been shown to be a strong predictor of early mortality [5,6]. EOV gained significance in the prognosis of especially patients with HF and researchers now suggest to integrate this parameter in prognostic risk scores [6–8]. This strong predictive pattern characterized by hypo- and hyperventilation during exercise appears especially in HF [9], however it is also described in other populations [10–16] and even in apparently healthy subjects [17]. It is therefore unclear if EOV is related to any cardiac pathology or if there is a general underlying pathophysiology. Up until now, studies explaining the possible pathophysiology of EOV suggest that this parameter could be related to increased circulatory delay, pulmonary congestion, disturbances in ergoreflex signalling and an increased chemosensitivity [8,18]. Especially the latter is known as the pathophysiologic explanation of the appearance of other abnormal breathing patterns such as periodic breathing (PB) [19], characterized by oscillations in VE during rest, and Cheyne-Stokes respiration (CSR) [20], characterized by oscillations in VE during

☆ Acknowledgement of grant support: This proof-of-concept study was funded by the University of Antwerp (FFI150117) and Cortex®, Leipzig, Germany.
☆☆ Conflicts of interest: The researchers confirm that there was no conflict of interest since the company did not interfere in the research nor in the development of the tool.
* Corresponding author at: University of Antwerp, Faculty of Medicine and Health Sciences, CDE S0.22, Universiteitsplein 1, 2610 Wilrijk, Belgium.
E-mail address: Justien.Cornelis@uantwerpen.be (J. Cornelis).
[1] These authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijcard.2016.12.159
0167-5273/© 2016 Elsevier Ireland Ltd. All rights reserved.

Please cite this article as: J. Cornelis, et al., Development of a clinical applicable graphical user interface to automatically detect exercise oscillatory ventilation: The VOdEX-..., Int J Cardiol (2016), http://dx.doi.org/10.1016/j.ijcard.2016.12.159

sleep [21–23]. It was seen that inspiration of oxygen evokes a decrease in chemosensitivity and abolishes the oscillatory breathing pattern [21,24]. It should be stated that PB, CSR and EOV are disorders of breathing control that have a central neurological origin [21]. Since the pathophysiology of EOV is not yet fully understood, it is a challenge to find an adequate therapy. Currently, presentation of EOV has been seen as an indication for advanced disease severity [25] and therefore adjusted medication therapy is prescribed and even heart transplantation is considered [26]. However, it should be noted that up until now, EOV has been visually determined by the clinician instead of automatically calculated by CPET software packages [6,18,27]. This method of assessment could enhance bias and EOV could be left unnoticed in many cases. Moreover, many different CPET systems are available with each its unique software for data analysis and data sampling. Due to the wide variety in data analysis, sampling, averaging and protocol, there could be a misbalance in the assessment of EOV. Because presence of EOV is based on pattern recognition, these assessment methods using CPET should be standardized. Moreover, no gold standard is available in defining EOV [27] and it was seen that the applied definition influenced the results significantly [5]. Despite the fact that the ESC guidelines prefer the use of the EOV-description as proposed by Corrà et al. [26,28], diligence and carefulness tell us that due to the lack of comparative research, it is unclear which definition is the most accurate at this moment. Therefore, four definitions [29–32] describing original characteristics have been put forward [9,27].

The goal of this proof-of-concept was to develop a clinical applicable graphical user interface (GUI) in which the current available definitions of EOV were integrated. It was the purpose to standardize the data sampling from the CPET device by implementing an uniform averaging filter on the raw breath-by-breath VE data. This would make it possible to detect EOV automatically and more standardized in each CPET.

2. Methods

The graphical user interface (GUI) was developed and designed in Matlab2013a (Mathworks, Massachusetts, USA). The raw breath-by-breath minute ventilation (VE) data of standardized (bicycle mode, ramp protocol, 3 min rest, 8–12 min exercise, 3 min recovery) conducted cardiopulmonary exercise tests (CPET) were imported in Matlab2013a using an Excel (Microsoft, Redmond, USA) format file. The VE against time curves were plotted. In order to apply the definitions on the data, the graphic is needed to be smoothed by selecting the adequate filter method. The optimal filter method to remove the noise from the collected breath-by-breath ventilation (VE) (l/min) CPET data was determined [33] by applying different filtering methods, as available in the CPET device, on the VE data in the Excel file [7, 16, 26, 27, 30, 34–36]. Since the VE curves did not represent a sinusoidal wave, the wavelet toolbox available in Matlab2013a was considered and consulted in order to select the appropriate wavelet transformation to smooth the data. The team, consisting out of four engineer students in their master's degree, assessed the available wavelet transformations in Matlab2013a and classified them into four categories i.e. down sampling (filter is too strong which evokes transformation of the original signal), insufficient noise suppression (filter is too weak and therefore too many noise is still present in the signal), data loss (filter is too strong and true signal is filtered) and appropriate transformations. A transformation was classified as appropriate if there was a balance seen in cancellation of noise and maintenance of true signal. This classification was done upon visual consideration (Fig. 1). The appropriate transformations were presented to the whole team i.e. the authors of this article and specialized clinicians, and decision of the most appropriate wavelet transformation was done by mediation. Ultimately, the selected wavelet transformation was repeated in order to separate the high frequency noise from the low frequency signal thus providing the best smoothing relative to preserved information [33] (Fig. 2).

Since there was no gold standard definition available, it was decided to program the four main definitions [29–32], representing the original characteristics of EOV. Furthermore, since the definition of Corrà et al. [26] was already proposed by the ESC guidelines [28], it was opted to implement this instead of the definition as suggested by Kremser et al. [29]. The only difference between both descriptions is the time the oscillations are present, respectively during 60% [26] and 66% [29] of the total CPET time. An overview of the implemented characteristics and definitions is provided in Table 1. The specific components of the descriptions had to be estimated. A peak detection algorithm, peakdet (x,d) function ('x' represents the signal, 'd' represents the threshold defining the minima and maxima values), starting and ending consistently with a local minimum, was integrated. Local minimum values (nadirs) and local maximum values (peaks) were detected and visualised by a cross (X). The oscillation cycle length was described as the distance between two consecutive minima using the linear line expression formula ($y = ax + b$). The base point, represented by a dot, was specified as the projection of the local maximum on the cycle length. The height of the oscillation (amplitude) was defined as the distance between the local maximum and the corresponding base point and was illustrated by a square (Fig. 3).

A database was developed which contains CPET data in a standard format of patients who provided informed consent, combined with specific patient identification parameters, and was connected to the GUI.

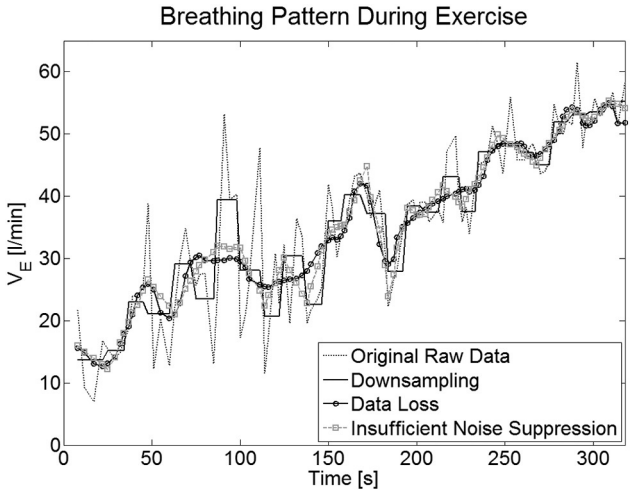


Fig. 1. Visual assessment of the most appropriate wavelet transformation.

3. Results

In order to average the data, the available filter methods in the CPET device were visually compared, however they provided ambiguous results towards data-loss suggesting depletion of true signal. It was the goal of this research to provide a standardized optimal filter method without loss of data. Since the VE curves did not represent a sinusoidal wave, the wavelet toolbox available in Matlab2013a was consulted. The search for the best filter method led to the selection of eight appropriate transformations. The team concluded by mediation that the Discrete Meyer wavelet transformation was the most suitable filter method. Level two was considered to provide the best smoothening (Fig. 2). Therefore, all breath-by-breath VE CPET data were filtered using Discrete Meyer Level 2 wavelet transformation.

In the α-version of the GUI, the characteristics of the four definitions (Table 1) were separately implemented by using the following criteria: (1) At least two or three consecutive amplitudes had to reach the ≥5 l/min reference value, (2) The cyclic pattern had to be present

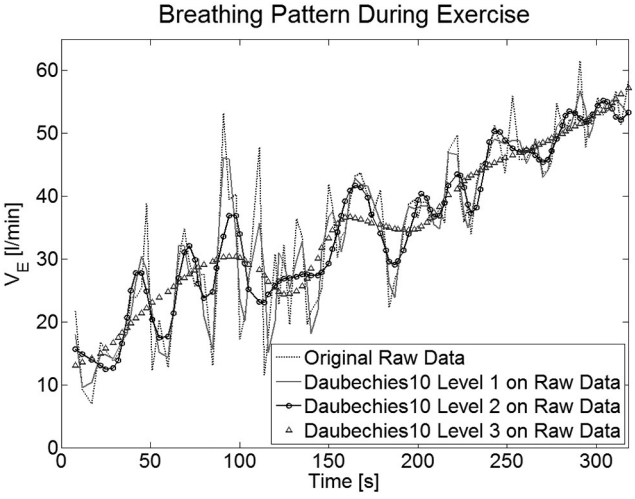


Fig. 2. Visual assessment of the most appropriate level of data smoothening.

Please cite this article as: J. Cornelis, et al., Development of a clinical applicable graphical user interface to automatically detect exercise oscillatory ventilation: The VOdEX-..., Int J Cardiol (2016), http://dx.doi.org/10.1016/j.ijcard.2016.12.159

Table 1
Description of the characteristics of the definitions implemented in the graphical user interface to determine EOV.

Author	Total duration of the oscillations during exercise	Cycle length of the oscillation	Amplitude of the oscillation	Regular oscillations	Other
Kremser et al. [29]	>66% of the total CPET time	–	>15% of the average value at rest	–	–
Corra et al. [26]	>60% of the total CPET time	–	>15% of the average value at rest	–	–
Leite et al. [31]	–	SD of ≥3 consecutive cycle lengths was within 20% of average	≥5 l/min each oscillation	≥3 regular oscillations	–
Ben-Dov et al. [30]	–	30–60s	≥25% of the mean VE value	≥2 regular oscillations	–
Sun et al. [32]	–	40–140 s	>30% of the mean VE value	≥3 regular oscillations	Oscillations had to be visible in ≥3 other CPET parameters

CPET: cardiopulmonary exercise test; VE: ventilation (l/min); SD: standard deviation.

≥66% of the total exercise time, (3) Cycle length may only deviate 20% of the mean of the three latest cycle lengths or had to be between 40 and 140 s. These characteristics were mutually combined to meet the four different definitions (Fig. 4). According to these criteria, the GUI could automatically analyse the VE curve and classify the CPET file into EOV present or absent. This was done for all four definitions separately. In this α-version of the GUI, each Excel file had to be introduced separately and selection of VE data and time data had to be introduced manually. The GUI was made adjustable for clinical research by creating sliders for the separate characteristics i.e. duration of the oscillations during CPET, amplitude, cycle length and number of regular oscillations. This way it is possible for the clinician or researcher to adjust the definition e.g. from an amplitude of ≥5 l/min [31] to an amplitude of ≥10 l/min and let the GUI recalculate so that an evaluation of different characteristics within the proposed definition is possible in the future.

Since the integrated characteristics did not entirely comply with the original definitions, the GUI was updated into a β-version, called the Ventilatory Oscillation during Exercise tool (VOdEX-tool), which could be translated into CPET software of the manufacturers. The rest and exercise data, detected by elevation of load, was recognized and separately assessed. Instead of the original characteristics [29], it was chosen to implement the first definition according to the ESC guidelines [26,28]. Therefore, the pattern had to be present for ≥60% of the total exercise time with adjusted amplitude of ≥115% of the average value at rest. If the resting phase was not measured, the amplitude was set at 5 l/min. According the second definition [31], EOV was present if the amplitude was ≥5 l/min in at least 3 consecutive regular (time of 2 consecutive nadirs within 20% of the average) oscillations. Thirdly, the amplitude of an oscillation was >30% of the average ventilation in at least 3 consecutive oscillations with a cycle length of 40–140 s [32]. Accordingly, oscillations were visible in three or more prognostic CPET variables. However, this GUI only investigates the VE data. Finally, the cycle length of an oscillation is 30–60 s and the amplitude was defined as peak–nadir ≥ mean VE during the cycle [30].

In this β-version, positive elements (i.e. basic standardized calculations, data averaging, flexibility towards research and clear clinical applicability) of the initial α-version are maintained. The major advantages are that (1) the four original definitions are correctly implemented as proposed by the authors, (2) the VOdEX-tool is connected to a database which allows analysis of bulk data at once and (3) the tool could be integrated in the CPET software of the manufacturers allowing distribution.

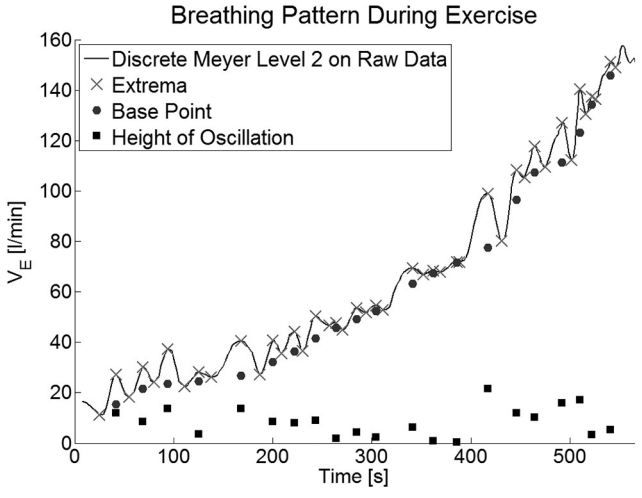


Fig. 3. Representation of the characteristics of the definitions. A cross represents local nadirs and peaks. The base point is visualised with a dot. The amplitude is illustrated by a square.

4. Discussion

Abnormal breathing patterns and increased ventilatory response to exercise associated with deregulation of the chemoreflex often occur in patients with HF [21,23,37]. These unusual curves in VE can be seen during sleep (CSR) [20,38], at rest (PB) [19,39] or solely during exercise (EOV) [40,42]. Especially EOV is associated with severity in prognosis and gained notice during recent years as plausible the most important prognostic parameter to register during CPET [5,6,9,25]. Despite the clinical importance of immediate EOV-detection, the assessment is still based on visual determination of the specialized clinician or researcher [27]. This is a lengthy task, which could be biased. This heterogeneity is illustrated by the wide interval of EOV prevalence in heart failure which was estimated between 7% [25,43] and 64% [44]. The reason to conduct this study was to develop and provide a tool (VOdEX-tool) that automatically assesses EOV, based on the original definitions and with a standardized data averaging, which could be made readily available for clinical use in each CPET assessment.

In order to smooth the EOV signal, various specific CPET software averaging methods e.g. 10-s moving average [16], 30-s average [34], 8-breath moving average [30], 5-breath moving average [35], one minute average [36] or undefined [7,26] were used [27]. This wide spectrum of filters applied to smooth the VE curve, contributes to different visualisation of the data. To provide an example, applying a one-minute averaging filter on an oscillatory VE pattern could flatten the curve extensively (by deleting too much information) in a way that a steadily increasing nearly normal VE pattern is seen instead of oscillations. This was also illustrated by applying the other standardized CPET filters. Therefore, a uniform applicable data-averaging filter had to be selected and implemented. Fourier, the dominant analytic tool in domain transformation, assumes the signal is stationary [33,45,46] while EOV is a rather non-stationary signal [47]. Therefore, implementation of wavelet transformation was chosen [33]. It was opted to use discrete wavelet analysis rather than continuous wavelet analysis [48]. The final wavelet transformation, discrete Meyer Level 2, was determined

Please cite this article as: J. Cornelis, et al., Development of a clinical applicable graphical user interface to automatically detect exercise oscillatory ventilation: The VOdEX-..., Int J Cardiol (2016), http://dx.doi.org/10.1016/j.ijcard.2016.12.159

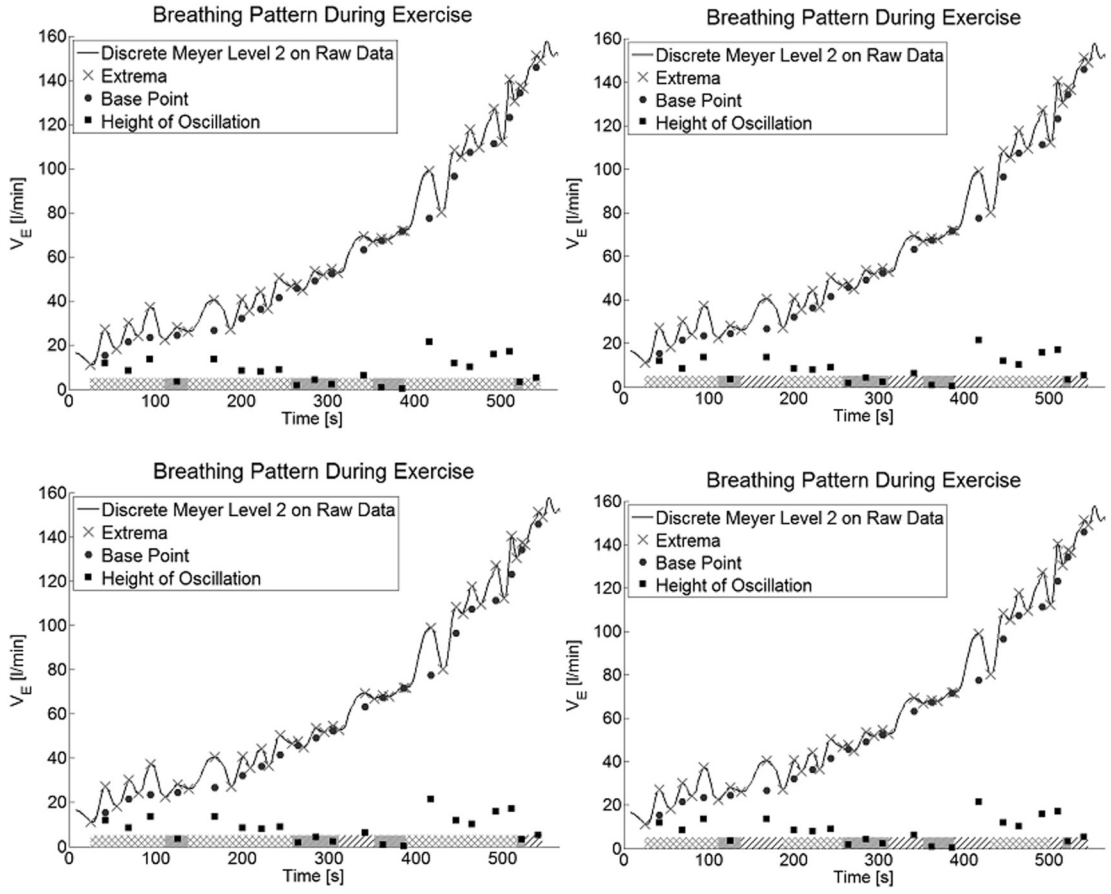


Fig. 4. Example of the VOdEX-tool results. Breath-by-breath bicycle (ramp 40 W (↑20 W/min); 8–12 min) CPET data (MetaMax3B; Cortex, Leipzig, Germany) of a male HF patient was retrospectively selected in the database. Four definitions (I–IV) assessed automatically EOV. Zones were crosshatched if the oscillations fulfilled the criteria of EOV. Otherwise, the band was hatched (partially fulfilled) or grey (not fulfilled).

by experiment and limited to the available wavelet toolbox in Matlab2013a. It cancels the noise (extreme data-points) of the CPET device without deleting the true VE signal. In that way, the VE data are smoothened and can be visually and automatically interpreted. If the amount of noise the CPET device produces could be quantified, more accurate methods could be applied to smooth the signal. Care should be taken when comparing data from one CPET device to another as automated CPET systems sometimes have become a "black box" [49]. This means that clinicians can easily interpret and understand the data, despite the implemented algorithms are not clarified by the manufacturer [49]. Therefore, it was opted to select one wavelet filter that could be applied in different CPET software. Despite CPET has been seen as the gold standard method to assess the exercise capacity [49] and prognosis in HF [28], it is a rather expensive method and it requests experience. Therefore, CPET could be underused in certain clinical settings [50,51]. To overcome this problem, detection of EOV using a thermal flowmeter was constructed by the group of Fu et al. [50]. Whether this wearable device is as effective in identifying EOV compared to standardized CPET assessment, still requests more research.

Besides implementing the most accurate data averaging method, also the characteristics of the available definitions for EOV had to be integrated in the tool in order to assess the VE curve automatically. Since no gold standard definition was available to describe EOV, the VOdEX-tool was designed to assess EOV by using the four most original definitions [26, 30–32]. The characteristics i.e. cycle length, amplitude, regularity and total duration of EOV were programmed as accurate as possible. However, mathematical inconsistency in the description of these characteristics by the previous referred authors provided ambiguous interpretations. For example, it was unclear if ≥60% referred to the whole exercise or only the beginning [52]. Moreover, original description of mathematical properties such as cycle length (EOV was present ≥60% [26] of the time versus three consecutive oscillations [31]) and amplitude (≥115% of the average value at rest [26] versus ≥5 l/min [31]) were not consistent and some cut-offs were rigorous. It is also ambiguous how these characteristics and cut-offs were initially established. Until now, it is therefore uncertain which definition is superior to assess EOV. To overcome this problem and to be able to conduct research towards the most adequate definition, the four definitions were integrated as accurate as possible and moreover the tool provides the option to adjust the cut-offs using a slider. The slider makes it possible for the clinician to adjust the criteria for each characteristic and allows estimating that effect on the presence of EOV. This is important in order to assess the most objective definition for EOV and to obtain a reliable gold standard definition in the future. Other parameters such as the slope of the curve and the linear regression could be added [50], along with possible quantification [45] of the EOV pattern. Moreover, integration of innovative new formulas could easily be introduced within the VOdEX-tool. A major advantage is that the tool is connected to a database, which allows analysis of multiple data files at once by making fast assessments and detections of EOV possible completely independent from any definition used. The automatic assessment takes little time and decreases risk of bias when compared to manual or visual calculation. Implementing the VOdEX-tool in existing CPET software allows the clinician and researcher to assess EOV in every conducted CPET. This way, the tool contributes to a fast, easy and standardized assessment of a highly prognostic CPET parameter.

4.1. Limitations and future directions

This article reports on the development of a tool to automatically assess EOV based on only four actually known and implemented

Please cite this article as: J. Cornelis, et al., Development of a clinical applicable graphical user interface to automatically detect exercise oscillatory ventilation: The VOdEX-..., Int J Cardiol (2016), http://dx.doi.org/10.1016/j.ijcard.2016.12.159

ARTICLE IN PRESS

definitions. Whether other definitions are more adequate to describe EOV, still have to be investigated. Fortunately, the VOdEX-tool is constructed in such a way that it allows integration of other characteristics in the future in order to enclose more reliable or perhaps even gold standard definitions. A major advantage of the tool is that selecting the most accurate discrete wavelet filter standardized data averaging. As mentioned in the discussion, selection of the appropriate filter was limited to the available wavelets in the matlab2013a toolbox. A more accurate calculation of the best filter method could be made in further research. Integrating this standardized automatic tool into CPET software, allows fast and continuous clinical assessment of EOV. That way it will be possible to assess EOV more standardized in every population learning more about the possible pathophysiology and estimating prevalence of this abnormal breathing pattern more accurately. It should be noted that validity but especially reliability of the tool should be subject of future investigation. To learn more about the different descriptions of EOV, validity could be estimated by comparing them with the definition provided in the guidelines [26,28]. To estimate reliability, assessment of EOV could be done by visual determination and could be compared to the detection of EOV by the VOdEX-tool in all CPET files in which VE is measured breath-by-breath.

5. Conclusions

The VOdEX-tool gives the possibility to overview the results of existing formulae for EOV at a glance. It is designed to assess EOV in a bulk standardized dataset at once and to extend the analyses with other definitions, cut-offs and interpretations. It is a tool for clinical and research purpose, allowing flexible analysis of EOV. The VOdEX-tool could be integrated in existing CPET software making computerized analysis readily available in clinical practice and therefore enhancing diagnostic and prognostic assessment of patients.

Conflict of interest

This proof-of-concept study was funded by the University of Antwerp and Cortex®, Leipzig, Germany. The researchers confirm that there was no conflict of interest since the company did not interfere in the research nor in the development of the tool. A request for a patent is pending.

Acknowledgements

The authors would like to thank Kris Poppe (Ir), Quinten Claes (Ir), Michel Deconinck (Ir) and Toon Van Assche (Ir), who were master students at the faculty of applied engineering (Antwerp, Belgium). They suggested the α-version of the GUI as a result of their assignment.

References

[1] C.W. Yancy, M. Jessup, B. Bozkurt, J. Butler, D.E. Casey, M.H. Drazner, et al., 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, Circulation 128 (16) (October 15 2013) e240–e327 (2013).
[2] P. Ponikowski, A.A. Voors, S.D. Anker, H. Bueno, J.G. Cleland, A.J. Coats, et al., 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC, Eur. Heart J. 37 (27) (Jul 14 2016) 2129–2200 (PubMed PMID: 27206819. Epub 2016/05/22. Eng).
[3] A. Mosterd, A.W. Hoes, Clinical epidemiology of heart failure, Heart 93 (9) (2007) 1137–1146.
[4] J. Cornelis, C. Vrints, C. Vanroy, D. Vissers, P. Beckers, Established prognostic exercise variables in heart failure, J. Card. Fail. 15 (Jul 2016) (PubMed PMID: 27427219. Epub 2016/07/19. Eng).
[5] J. Cornelis, J. Taeymans, W. Hens, P. Beckers, C. Vrints, D. Vissers, Prognostic respiratory parameters in heart failure patients with and without exercise oscillatory ventilation—a systematic review and descriptive meta-analysis, Int. J. Cardiol. 182 (2015) 476–486.
[6] L.P. Cahalin, P. Chase, R. Arena, J. Myers, D. Bensimhon, M.A. Peberdy, et al., A meta-analysis of the prognostic significance of cardiopulmonary exercise testing in patients with heart failure, Heart Fail. Rev. 18 (1) (Jan 2013) 79–94 (PubMed PMID: 22733204. Epub 2012/06/27. eng).
[7] P. Agostoni, U. Corrà, G. Cattadori, F. Veglia, R. La Gioia, A.B. Scardovi, et al., Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: a multiparametric approach to heart failure prognosis, Int. J. Cardiol. 167 (2013) 2710–2718 (2013).
[8] R. Malhotra, K. Bakken, E. D'Elia, G.D. Lewis, Cardiopulmonary exercise testing in heart failure, JACC Heart Fail. (2016).
[9] U. Corra, Exercise oscillatory ventilation in heart failure, Int. J. Cardiol. 206 (Suppl) (Mar 2016) S13–S15 (PubMed PMID: 26935880. Epub 2016/03/05. eng).
[10] S. Vangesselen, M. Weymans, L. Mertens, M. Gewillig, T. Reybrouck, et al., Comput. Methods Prog. Biomed. 80 (1) (Oct 2005) 89–92 (PubMed PMID: WOS: 000232754300009).
[11] K. Miyagi, H. Asanoi, S. Ishizaka, T. Kameyama, S. Sasayama, Limited value of anaerobic threshold for assessing functional capacity in patients with heart failure, Clin. Cardiol. 16 (2) (Feb 1993) 133–137 (PubMed PMID: 8435926. Epub 1993/02/01. eng).
[12] A. Koike, N. Shimizu, A. Tajima, T. Aizawa, L.T. Fu, H. Watanabe, et al., Relation between oscillatory ventilation at rest before cardiopulmonary exercise testing and prognosis in patients with left ventricular dysfunction, Chest 123 (2) (Feb 2003) 372–379 (PubMed PMID: 12576354. Epub 2003/02/11. eng).
[13] J. Kato, A. Koike, M. Hoshimoto-Iwamoto, O. Nagayama, K. Sakurada, A. Sato, et al., Relation between oscillatory breathing and cardiopulmonary function during exercise in cardiac patients, Circ. J. 77 (3) (2013) 661–666.
[14] T. Okumura, A. Hirashiki, S. Yamada, R. Okamoto, N. Shinoda, Y. Kono, et al., (Eds.), Prognostic value and mechanisms of exercise oscillatory ventilation in patients with idiopathic dilated cardiomyopathy, European Heart Journal, Oxford Univ Press, Great clarendon St, oxford OX2 6DP, England, 2011.
[15] J. Muneuchi, K. Joo, K. Yamamura, M. Watanabe, E. Morihana, Y. Imoto, et al., Exertional oscillatory ventilation during cardiopulmonary exercise test in Fontan patients with total cavopulmonary connection, Pediatr. Cardiol. 30 (4) (May 2009) 452–457 (PubMed PMID: 19066761. Epub 2008/12/11. eng).
[16] R. Neviere, J.L. Edme, D. Montaigne, E. Boleslawski, F.R. Pruvot, S. Dharancy, Prognostic implications of preoperative aerobic capacity and exercise oscillatory ventilation after liver transplantation, Am. J. Transplant. 14 (1) (Jan 2014) 88–95 (PubMed PMID: WOS:000328597900013).
[17] M. Guazzi, R. Arena, M. Pellegrino, F. Bandera, G. Generati, V. Labate, et al., Prevalence and characterization of exercise oscillatory ventilation in apparently healthy individuals at variable risk for cardiovascular disease: a subanalysis of the EURO-EX trial, Eur. J. Prev. Cardiol. 23 (3) (Feb 2016) 328–334 (PubMed PMID: 25868603. Epub 2015/04/15. eng).
[18] B.P. Dhakal, R.M. Murphy, G.D. Lewis, Exercise oscillatory ventilation in heart failure, Trends Cardiovasc. Med. 22 (7) (2012 Oct) 185–191 (PubMed PMID: 23062973. Epub 2012/10/16. eng).
[19] S.A. Sands, Y. Mebrate, B.A. Edwards, S. Nemati, C.H. Manisty, A.S. Desai, et al., Resonance as the mechanism of daytime periodic breathing in patients with heart failure, Am. J. Respir. Crit. Care Med. (Aug 25 2016) (PubMed PMID: 27559818. Epub 2016/08/26. Eng).
[20] S. Javaheri, A mechanism of central sleep apnea in patients with heart failure, N. Engl. J. Med. 341 (1999) 949–954 (1999).
[21] A.S. Coats (Ed.), SERVE-HF-Was Treating a Central Neurological Disturbance of Breathing Control by a Mechanism Initially Designed to Keep Open an Obstructed Airway Always Doomed to Fail?, International Cardiovascular Forum Journal, 2015.
[22] Y. Tomita, T. Kasai, T. Kisaka, H.B. Rossiter, Y. Kihara, K. Wasserman, et al., Altered breathing syndrome in heart failure: newer insights and treatment options, Curr. Heart Fail. Rep. 12 (2) (2015) 158–165.
[23] M. Plataki, S.A. Sands, A. Malhotra, Clinical consequences of altered chemoreflex control, Respir. Physiol. Neurobiol. 189 (2) (11/1/2013) 354–363.
[24] D.P. Francis, K. Willson, L.C. Davies, A.J.S. Coats, M. Piepoli, Quantitative general theory for periodic breathing in chronic heart failure and its clinical implications, Circulation 102 (18) (Oct 31 2000) 2214–2221 (PubMed PMID: WOS:000090109400019).
[25] L.J. Olson, A.M. Arruda-Olson, V.K. Somers, C.G. Scott, B.D. Johnson, Exercise oscillatory ventilation: instability of breathing control associated with advanced heart failure, Chest 133 (2) (Feb 2008) 474–481 (PubMed PMID: 18071013. Pubmed Central PMCID: 2768383).
[26] U. Corra, A. Giordano, E. Bosimini, A. Mezzani, M. Piepoli, A.J. Coats, et al., Oscillatory ventilation during exercise in patients with chronic heart failure: clinical correlates and prognostic implications, Chest 121 (5) (May 2002) 1572–1580 (PubMed PMID: 12006446. Epub 2002/05/15. eng).
[27] J. Cornelis, P. Beckers, C. Vanroy, T. Volckaerts, C. Vrints, D. Vissers, An overview of the applied definitions and diagnostic methods to assess exercise oscillatory ventilation—a systematic review, Int. J. Cardiol. 190 (2015) 161–169.
[28] G.J. Balady, R. Arena, K. Sietsema, J. Myers, L. Coke, G.F. Fletcher, et al., Clinician's guide to cardiopulmonary exercise testing in adults a scientific statement from the American Heart Association, Circulation 122 (2) (Jul 13 2010) 191–225 (PubMed PMID: WOS:000279801700013).
[29] C.B. Kremser, M.F. O'Toole, A.R. Leff, Oscillatory hyperventilation in severe congestive heart failure secondary to idiopathic dilated cardiomyopathy or to ischemic cardiomyopathy, Am. J. Cardiol. 59 (8) (Apr 1 1987) 900–905 (PubMed PMID: 3825954. Epub 1987/04/01. eng).
[30] I. Ben-Dov, K.E. Sietsema, R. Casaburi, K. Wasserman, Evidence that circulatory oscillations accompany ventilatory oscillations during exercise in patients with heart failure, Am. Rev. Respir. Dis. 145 (4 Pt 1) (Apr 1992) 776–781 (PubMed PMID: 1554201. Epub 1992/04/01. eng).

Please cite this article as: J. Cornelis, et al., Development of a clinical applicable graphical user interface to automatically detect exercise oscillatory ventilation: The VOdEX-..., Int J Cardiol (2016), http://dx.doi.org/10.1016/j.ijcard.2016.12.159

ARTICLE IN PRESS

[31] J.J. Leite, A.J. Mansur, H.F. de Freitas, P.R. Chizola, E.A. Bocchi, M. Terra-Filho, et al., Periodic breathing during incremental exercise predicts mortality in patients with chronic heart failure evaluated for cardiac transplantation, J. Am. Coll. Cardiol. 41 (12) (Jun 18 2003) 2175–2181 (PubMed PMID: 12821243. Epub 2003/06/25. eng).
[32] X.G. Sun, J.E. Hansen, J.F. Beshai, K. Wasserman, Oscillatory breathing and exercise gas exchange abnormalities prognosticate early mortality and morbidity in heart failure, J. Am. Coll. Cardiol. 55 (17) (Apr 27 2010) 1814–1823 (PubMed PMID: 20413031).
[33] R. Merry, Wavelet Theory and Applications: A Literature Study, 2005.
[34] M. Guazzi, R. Arena, A. Ascione, M. Piepoli, M.D. Guazzi, Exercise oscillatory breathing and increased ventilation to carbon dioxide production slope in heart failure: an unfavorable combination with high prognostic value, Am. Heart J. 153 (5) (May 2007) 859–867 (PubMed PMID: 17452165. Epub 2007/04/25. eng).
[35] T. Yajima, A. Koike, K. Sugimoto, Y. Miyahara, F. Marumo, M. Hiroe, Mechanism of periodic breathing in patients with cardiovascular disease, Chest 106 (1) (Jul 1994) 142–146 (PubMed PMID: 8020261. Epub 1994/07/01. eng).
[36] R.M. Murphy, R.V. Shah, R. Malhotra, P.P. Pappagianopoulos, S.S. Hough, D.M. Systrom, et al., Exercise oscillatory ventilation in systolic heart failure: an indicator of impaired hemodynamic response to exercise, Circulation 124 (13) (Sep 27 2011) 1442–1451 (PubMed PMID: 21875912. Pubmed Central PMCID: 3415253).
[37] T.D. Bradley, The ups and downs of periodic breathing: implications for mortality in heart failure, J. Am. Coll. Cardiol. 41 (12) (6/18/2003) 2182–2184.
[38] S. Javaheri, J.A. Dempsey, Mechanisms of sleep apnea and periodic breathing in systolic heart failure, Sleep Med. Clin. 2 (4) (12 2007) 623–630.
[39] T.P. Olson, R.P. Frantz, E.M. Snyder, K.A. O'Malley, K.C. Beck, B.D. Johnson, Effects of acute changes in pulmonary wedge pressure on periodic breathing at rest in heart failure patients, Am. Heart J. 153 (1) (Jan 2007) (PubMed PMID: WOS: 000243706000022).
[40] P. Agostoni, A. Apostolo, R.K. Albert, Mechanisms of periodic breathing during exercise in patients with chronic heart failure, Chest 133 (1) (Jan 2008) 197–203 (PubMed PMID: 18187746).
[42] E. Hermand, F.J. Lhuissier, N. Voituron, J.P. Richalet, Ventilatory oscillations at exercise in hypoxia: a mathematical model, J. Theor. Biol. 411 (Oct 12 2016) 92–101 (PubMed PMID: 27743839. Epub 2016/10/25. Eng).
[43] U. Corra, A. Mezzani, A. Giordano, E. Bosimini, P. Giannuzzi, Exercise haemodynamic variables rather than ventilatory efficiency indexes contribute to risk assessment in chronic heart failure patients treated with carvedilol, Eur. Heart J. 30 (24) (Dec 2009) 3000–3006 (PubMed PMID: 19406866. Epub 2009/05/02. eng).
[44] T.Y. Chon, B.D. Johnson, R.F. Rea, A.C. Clavell, V.K. Somers, D.L. Hayes, et al., Cardiac resynchronization therapy attenuates exercise periodic breathing in patients with advanced heart failure, J. Card. Fail. 10 (4) (Aug 2004) S65 (PubMed PMID: WOS: 000223857900172).
[45] T.P. Olson, B.D. Johnson, Quantifying oscillatory ventilation during exercise in patients with heart failure, Respir. Physiol. Neurobiol. 190 (Jan 1 2014) 25–32 (PubMed PMID: 24121091).
[46] E. Hermand, F.J. Lhuissier, J. Larribaut, A. Pichon, J.P. Richalet, Ventilatory oscillations at exercise: effects of hyperoxia, hypercapnia, and acetazolamide, Phys. Rep. 3 (6) (Jun 2015) (PubMed PMID: 26109194. Pubmed Central PMCID: PMC4510637. Epub 2015/06/26. Eng).
[47] J.S. Walker, A Primer on Wavelets and Their Scientific Applications, CRC press, 1999.
[48] P. Barralon, N. Vuillerme, N. Noury, Walk detection with a kinematic sensor: frequency and wavelet comparison, Conf. Proc. Annu. Int. Conf. IEEE Eng. Med. Biol. Soc. IEEE Eng. Med. Biol. Soc. Conf. 1 (2006) 1711–1714 (PubMed PMID: 17945661. Epub 2007/10/20. eng).
[49] L. Hodges, D. Brodie, P. Bromley, Validity and reliability of selected commercially available metabolic analyzer systems, Scand. J. Med. Sci. Sports 15 (5) (2005) 271–279.
[50] T.-C. Fu, W.-C. Lin, J.-S. Wang, C.-H. Wang, C.-T. Chang, C.-L. Tsai, et al., Detection of exercise periodic breathing using thermal flowmeter in patients with heart failure, Med. Biol. Eng. Comput. 1-10 (2016).
[51] D.E. Forman, J. Myers, C.J. Lavie, M. Guazzi, B. Celli, R. Arena, Cardiopulmonary exercise testing: relevant but underused, Postgrad. Med. 122 (6) (2010) 68–86.
[52] M. Guazzi, J. Myers, M.A. Peberdy, D. Bensimhon, P. Chase, R. Arena, Exercise oscillatory breathing in diastolic heart failure: prevalence and prognostic insights, Eur. Heart J. 29 (22) (Nov 2008) 2751–2759 (PubMed PMID: 18836201).

Please cite this article as: J. Cornelis, et al., Development of a clinical applicable graphical user interface to automatically detect exercise oscillatory ventilation: The VOdEX-..., Int J Cardiol (2016), http://dx.doi.org/10.1016/j.ijcard.2016.12.159