RE: Letter regarding the article “Additive prognostic value of left ventricular systolic dysfunction in a population-based cohort”

Nicolas Duchateau and Bart Bijnens
Published on November 9, 2016

Published on November 9, 2016

RE: Letter regarding the article “Additive prognostic value of left ventricular systolic dysfunction in a population-based cohort”

Nicolas Duchateau, Associate Professor, CREATIS UMR 5220 – Université Lyon 1, France
Other Contributors:
Bart Bijnens, ICREA Research Professor

> We have read with interest the study from Kuznetsova et al. published recently in Circulation: Cardiovascular Imaging, which provides additional evidence on the superiority of peak global longitudinal strain (GLS) over ejection fraction and traditional cardiovascular risk factors [1]. The authors notably analyzed a large population of 791 subjects, using commercial 2D speckle-tracking tools in a single 4-chamber view. They show higher prognostic value of GLS after adjusting for conventional risk factors, as well as LV mass index and TDI e’ velocity. Of additional interest, the study reports that the risk for cardiovascular events increases with the number of LV abnormalities (low GLS, diastolic dysfunction, and hypertrophy), and confirms GLS as a complementary parameter for patient assessment and follow-up.
>
> Global strain and EF actually reflect similar information on cardiac function: the total deformation at end-ejection. Nonetheless, the contractility of the subendocardial fibers is more vulnerable to cardiac dysfunction, such that impaired longitudinal deformation is generally the initial manifestation as a result of the transmural fiber arrangement [2]. This impairment is initially compensated by increased circumferential deformation to maintain sufficient stroke volume. Thus, as confirmed in the study from Kuznetsova et al., the strain components (assessed independently) naturally represent more selective markers of cardiac dysfunction, with higher potential for prognosis [3,4].
>
> The study from Kuznetsova et al. relies on peak GLS, although distinction is made between the endocardial, midwall and epicardial layers (with roughly similar observations). For the scope of the study ---investigating trends between LV wall deformation and prognosis--- relying on global strain is relevant enough, given the large population and adjustments for potential confounding factors. Nonetheless, the reported GLS values and the proposed cut-offs should be considered with caution.
>
> Indeed, strain measurements are reliable within a ±5-10% margin (around ±1-2% in absolute terms) [5,6]. Although now standardized in commercial software, the analysis depends on many factors, among which endocardial delineation, image quality, frame rate, and platform-specific algorithms. Thus, the cut-off values reported for the prognostic ability of strain data should be regarded as indicative of a trend, but not as an unquestionable guideline to assess an individual patient. Besides, peaks are challenging to identify on multiple-peaked curves or in zones with very low deformation.
>
> A more comprehensive look at the echocardiographic images is therefore required to complement indicative trends on large populations and better understand individual behaviors. The temporal evolution along the cycle brings complementary information on the respective timings of each segment, to relate with the timings of cardiac activation and filling/emptying. Local strain alterations can be complemented with prior knowledge on the patient and the pathology, and data at complementary locations. Besides, spatiotemporal pattern visualization facilitates the detection of artifacts in lower imaging quality regions (mitral ring, apex, anterior wall), improving the reproducibility of measurements at these locations. Actually, academic researchers are now able to go beyond single cut-offs on these data and analyze the whole spatiotemporal patterns [7-12]. Statistical tools from computational anatomy reveal the relevant trends in these patterns, and quantify the distance between individuals and these modeled trends ---similar to the concepts of z-scores and statistical parametrical mapping, widely used to reveal abnormalities in neuroimaging studies.

Thus, in order to become truly useful in an individual, there is room for a more refined understanding of population trends, as a continuation of the analysis of global descriptors as in Kuznetsova et al. and related studies [3,4]. Situating the individual against the normal range and known etiologies of cardiac dysfunction can serve to highlight abnormalities of importance and better understand patient evolution with follow-up or therapy [13]. In the near future, the quantitative analysis of cardiac function should therefore go beyond simple quantitative descriptors such as EF and global strain. It should combine the advantages of (i) trend analysis on large populations, via simple descriptors and correction for confounding factors, and (ii) individual analysis that integrates both prior knowledge about the pathophysiology and information from multiple sources [14]. Advanced statistical and machine learning methods already exist to get an overall picture of multiple relevant descriptors on each individual [15,16], although they still need to be confirmed in larger populations. Besides, efficient ways to integrate the knowledge from the experienced clinical observer still need to be explored.

In summary, GLS can be robust and informative enough when dealing with larger cohorts, homogeneous patient groups, and tightly controlled images analysis by experienced operators. In this sense, it should replace EF in clinical trials evaluating prognosis. Nonetheless, for routine clinical practice on individuals, a stronger critical view is required, which integrates the reproducibility of measurements, the repeatability of observations in individuals and the small differences in cut-offs between groups with strongly different prognosis. Repeated assessment through the use of complementary tools, imaging modalities, and clinical information remains essential.

Sources of funding
The authors acknowledge the partial support from the Spanish Ministry of Economy and Competitiveness (grant TIN2014-52923-R and the Maria de Maeztu Units of Excellence Programme -MDM-2015-0502) and FEDER.

Disclosures
None.

References

1. Kuznetsova T, Cauwenberghs N, Knez J, Yang WY, Herbots L, D'hooge J, Haddad F, Thujs L, Voigt JU, Staessen JA. Additive prognostic value of left ventricular systolic dysfunction in a population-based cohort. Circ Cardiovasc Imaging. 2016;9:e004661. doi: 10.1161/CIRCIMAGING.116.004661.

2. Tan YT, Wenzelburger F, Lee E, Heatlie G, Leyva F, Patel K, Frenneaux M, Sanderson JE. The pathophysiology of heart failure with normal ejection fraction: exercise echocardiography reveals complex abnormalities of both systolic and diastolic ventricular function involving torsion, untwist, and longitudinal motion. J Am Coll Cardiol. 2009;54:36-46. doi: 10.1016/j.jacc.2009.03.037.

3. Choi EY, Rosen BD, Fernandes VR, Yan RT, Yoneyama K, Donekal S, Opdahl A, Almeida AL, Wu CO, Gomes AS, Bluemke DA, Lima JA. Prognostic value of myocardial circumferential strain for incident heart failure and cardiovascular events in asymptomatic individuals: the Multi-Ethnic Study of Atherosclerosis. Eur Heart J. 2013;34:2354-61. doi: 10.1093/eurheartj/eht133.

4. Cheng S, McCabe EL, Larson MG, Merz AA, Osypiuk E, Lehman BT, Stantchev P, Aragam J, Solomon SD, Benjamin EJ, Vasan RS. Distinct aspects of left ventricular mechanical function are differentially associated with cardiovascular outcomes and all-cause mortality in the community. J Am Heart Assoc. 2015;4:e002071. doi: 10.1161/JAHA.115.002071.

5. De Craene M, Marchesseau S, Heyde B, Gao H, Alessandrini M, Bernard O, Piella G, Porras AR, Tautz L, Hennemuth A, Prakosa A, Liebgott H, Somphone O, Allain P, Makram Ebeid S, Delingette H, Sermesant M, D'hooge J, Saloux E. 3D strain assessment in ultrasound (Straus): a synthetic comparison of five tracking methodologies. IEEE Trans Med Imaging. 2013;32:1632-46. doi: 10.1109/TMI.2013.2261823.

6. D'hooge J, Barbosa D, Gao H, Claus P, Prater D, Hamilton J, Lysyansky P, Abe Y, Ito Y, Houle H, Pedri S, Baumann R, Thomas J, Badano LP; EACVI/ASE/Industry Task Force to Standardize Deformation Imaging. Two-dimensional speckle tracking echocardiography:

standardization efforts based on synthetic ultrasound data. Eur Heart J Cardiovasc Imaging. 2016;17:693-701. doi: 10.1093/ehjci/jev197.

7. Chandrashekara R, Rao A, Sanchez-Ortiz GI, Mohiaddin RH, Rueckert D. Construction of a statistical model for cardiac motion analysis using nonrigid image registration. Proc. Inf Process Med Imaging, LNCS. 2003;2732:599-610. doi: 10.1007/978-3-540-45087-0_50.

8. Rougon N, Petitjean C, Preteux FJ. Building and using a statistical 3D motion atlas for analyzing myocardial contraction in MRI. Proc. SPIE Med Imaging. 2004:5370. doi:10.1117/12.535609.

9. Duchateau N, De Craene M, Piella G, Silva E, Doltra A, Sitges M, Bijnens BH, Frangi AF. A spatiotemporal statistical atlas of motion for the quantification of abnormal myocardial tissue velocities. Med Image Anal. 2011;15:316-28. doi: 10.1016/j.media.2010.12.006.

10. De Craene M, Duchateau N, Tobon-Gomez C, Ghafaryasl B, Piella G, Rhode KS, Frangi A. SPM to the heart: mapping of 4D continuous velocities for motion abnormality quantification. Proc. Int Symp Biomed Imaging. 2012:454-7. doi: 10.1109/ISBI.2012.6235582.

11. McLeod K, Sermesant M, Beerbaum P, Pennec X. Spatio-temporal tensor decomposition of a polyaffine motion model for a better analysis of pathological left ventricular dynamics. IEEE Trans Med Imaging. 2015;34:1562-75. doi: 10.1109/TMI.2015.2405579.

12. Bai W, Shi W, de Marvao A, Dawes TJ, O'Regan DP, Cook SA, Rueckert D. A bi-ventricular cardiac atlas built from 1000+ high resolution MR images of healthy subjects and an analysis of shape and motion. Med Image Anal. 2015;26:133-45. doi: 10.1016/j.media.2015.08.009.

13. Duchateau N, Doltra A, Silva E, De Craene M, Piella G, Castel MÁ, Mont L, Brugada J, Frangi AF, Sitges M. Atlas-based quantification of myocardial motion abnormalities: added-value for understanding the effect of cardiac resynchronization therapy. Ultrasound Med Biol. 2012;38:2186-97. doi: 10.1016/j.ultrasmedbio.2012.08.009.

14. Cikes M, Solomon SD. Beyond ejection fraction: an integrative approach for assessment of cardiac structure and function in heart failure. Eur Heart J. 2016;37:1642-50. doi: 10.1093/eurheartj/ehv510.

15. Shah SJ, Katz DH, Selvaraj S, Burke MA, Yancy CW, Gheorghiade M, Bonow RO, Huang CC, Deo RC. Phenomapping for novel classification of heart failure with preserved ejection fraction. Circulation. 2015;131:269-79. doi: 10.1161/CIRCULATIONAHA.114.010637.

16. Sanchez-Martinez S, Duchateau N, Erdei T, Fraser AG, Bijnens BH, Piella G. Characterization of myocardial motion patterns by unsupervised multiple kernel learning. Med Image Anal. 2017;35:70-82. doi: 10.1016/j.media.2016.06.007.

Show Less

Competing Interests: None declared.