Annals of Physical and Rehabilitation Medicine 64 (2021) 101504

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Editorial

The challenges of precision medicine in chronic low back pain: Lessons learned from active discopathy

"Without a diagnosis, all treatment is irrational". This statement from Hippocrates finds resonance when it comes to so-called « non-specific » low back pain (LBP) [1]. The diagnosis of non-specific LBP assumes that in the absence of a readily identifiable plausible nociceptive source or known pathoanatomical cause, there is none [1–4], and that carrying out clinical or imaging investigation is of low value and may cause harms [1]. We agree that investigating the causes of LBP is a challenge in daily practice and in research because: 1/contributors to both causes and consequences of LBP are heterogeneous: they include pathoanatomical factors, but also contextual factors, as defined by the International Classification of Functioning, Disability and Health [5], 2/clinical and imaging testing lacks specificity when considered in isolation, and 3/straightforward methods to fully validate their value as diagnosis and/or prognosis biomarkers are lacking.

Despite these challenges, we disagree that LBP should be left undiagnosed, namely under the umbrella of non-specific LBP, which may account for up to 90% of people with LBP, because this label is used by default and exposes to non-specific treatments, like positive health [3], or holistic pseudoscientific approaches. These treatments at best may not be harmful, at worse may promote misconceptions and misbeliefs, and cause harms in both patients and health care providers. Some authors recently promoted the idea to put efforts on reducing the impact of LBP on people's lives, rather than seeking medical treatment. At a time when all fields of health care and medicine are moving towards precision, namely personalized treatments and health care paths designed according to the complete phenotyping of patients, in all their dimensions, from body structures and functions, to personomics and exposomics, the non-specific conceptual approach to LBP and to musculoskeletal disorders, is surprising. More granularity is vital to determine which treatment is right for which patients [6,7].

In this issue of the Annals of Physical and Rehabilitation Medicine, Tavares and colleagues reported the results of a randomized trial of glucocorticoid intradiscal injection for people with chronic LBP and active discopathy (Modic 1 changes) [8]. The authors tested a treatment with a plausible short-term anti-inflammatory effect, in a selected group of 39 participants with chronic LBP, with a plausible relation to intervertebral disc inflammation. The authors confirmed their research hypothesis and found a reduction in pain at 1 month. Interestingly, despite variations in the study design and a small sample size, Tavares and colleagues succeeded in replicating the results of a large randomized trial, previously published in 2017, by Nguyen and colleagues, conducted in 135 participants with chronic LBP and active discopathy [9]. These results further confirm the relevance of targeting local inflammation in people with chronic LBP and active discopathy.

The significance of Modic 1 changes, as an imaging biomarker of a painful intervertebral disc, remains controversial [10]. It seems to gain specificity when considered along with clinical and biological biomarkers [11–13]. As for other biomarkers in LBP, straightforward methods to fully validate Modic 1 changes as a biomarker of a painful intervertebral disc are lacking, in the absence of a reliable gold standard. Provocative discography, which purpose is to determine whether increasing the intradiscal pressure elicits pain, has a high percentage of false-positive results, up to 25% [14,15]. This lack of gold standard methods of validation may lead to the emergence of unvalidated pain labels, poorly validated etiopathogenic hypotheses or inefficient targeted treatments. However, these consistently failed to be replicated by independent groups. In modern times, popular but unvalidated infectious origin of LBP and subsequent interest of anti-infectious treatments was suggested [16], but failed to be replicated by independent groups [17,18], similarly as the interest of intradiscal methylene blue in discogenic LBP [19,20]. In the challenging process of validating pain labels, etiologies or targeted treatments in the field of LBP, the study by Tavares and colleagues underlines the value of replicating similar findings by independent groups. In the past decades, several aspects of LBP associated with active discopathy have been consistently replicated by independent groups, including observations of a more frequent association with chronic LBP, poor long-term outcomes, inflammatory-like pain pattern and positive impact of treatments targeting local inflammation and adverse biomechanical factors [11,12]. Altogether, these findings contributed to improve the phenotyping of this subgroup of people with LBP, who would otherwise remain classified by default as non-specific, and to promote targeted treatments. However, even when a readily identifiable plausible nociceptive source is present, people with chronic LBP may have more than one cause of LBP, and phenotyping should also include dimensions of functioning other than pathoanatomy [6,7].

From a practical point of view, a rational approach to people with LBP should allow greater precision in diagnoses and treatments. From a research point of view, efforts in accurate and specific diagnosis of LBP are important in advancing research

https://doi.org/10.1016/j.rehab.2021.101504

and understanding regarding what is currently considered non-specific LBP. Advances made in the field of low back pain associated with active discopathy and replication of similar findings by independent groups may serve as a model of validation of phenotypes in people with LBP. These advances should be supported by methodological innovations allowing validation of phenotypes and assessment of therapeutic approaches stratified on phenotypes, in a more straightforward, but still rigorous manner.

Authors' contributions

Drafting of the present manuscript. All authors.
Final approval. All authors.

Disclosure of interest

Associate Professor Christelle Nguyen and Professor François Rannou are investigators in 2 trials assessing the interest of intradiscal therapies in chronic low back pain (NCT03737461, NCT03712527) and are authors of the following article reporting the results of the PREDID trial (NCT00804531): Nguyen C, Boutron I, Baron G, Sanchez K, Palazzo C, Benchimol R, et al. Intradiscal Glucocorticoid Injection for Patients With Chronic Low Back Pain Associated With Active Discopathy: A Randomized Trial. Ann Intern Med 2017;166:547-56.

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