Cancer pain is over! (If you want it)

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Introduction

1969. John Lennon and Yoko Ono surprised the world with their now legendary campaign, “War is over! (If you want it)”. This simple, yet powerful and provocative message, made when the Vietnam War was in full flow, relayed an incredible international pacifist movement that highlighted one thing: we can choose to stop the war, if that is what we want.

2022. Can we talk about a war on cancer pain? In the international literature on the subject, the expression is systematically repeated and very telling. While the incidence of cancer increases constantly [1], the figures for cancer pain do not improve. Despite considerable scientific and therapeutic progress, this has been the case for several decades [2, 3]. According to the World Health Organization, “In 2018, there were an estimated 18 million new cases of cancer and 10 million deaths from cancer worldwide. The predicted global burden will double to about 29–37 million new cancer cases by 2040, with the greatest increases in low- and middle-income countries” [1]. Given what we know about the prevalence of cancer pain, regardless of the stage of the disease as well as its presence in cancer survivors [2, 3], we are thus going to be faced with a real challenge in terms of public health, particularly as the inequalities between countries are already considerable [1]. All our articles on the subject deplore these figures and use them as the starting point for a problem of scale that we would like to resolve—once and for all—, in our role as healthcare professionals managing cancer pain, an issue that is still widely underestimated and undertreated, including in palliative situations [1–5]. Although many scientific articles focus on proposing

increasingly detailed and exhaustive models for understanding multimorphic cancer pain and trying to improve the situation that our cancer patients experience [6], there is still a gap between theory and real life, between scientific knowledge and its application in the field. In clinical practice, the multidisciplinary healthcare teams involved in supportive care still struggle daily to obtain early access to patients as a means of improving cancer pain management. But who or what are we fighting against? And what weapons do we have?

The lessons of the COVID pandemic

Recently, the COVID crisis plunged us all brutally into an unprecedented worldwide pandemic. Even though the epidemic is still present at the time of writing this article, science was able to adapt in a truly remarkable manner, including in emergency situations, making it possible to create, innovate, and find synergies to eradicate the problem both in terms of managing the health crisis and prevention, notably with treatment protocols and vaccines [7]. The key players in medicine and the healthcare sector in the broadest sense of the term showed society their remarkable agility and capacity for adaptation in the face of a brutal change that needed fast operational responses. In many countries, the public authorities implemented funding and healthcare strategies to stop the pandemic. Unfortunately, not all countries benefited from this efficiency because of their beliefs, for example, or the absence of political goodwill on the part of certain leaders, or low national economic levels. By definition, a virus is capable of mutating and adapting to its environment to survive; in parallel, this aptitude required a change at our level if we were to be able to resist at the societal level.

This was probably our first challenge when we evoked cancer pain: our aptitude to change in the face of a multimorphic nosological entity that has itself changed and is constantly changing [6, 8]. This involves our desire to change in order to adapt, succeed, and finally invert the curves and sustainably improve the quality of life of our patients.

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This COVID pandemic has notably demonstrated the importance of an international collaborative approach in terms of public health, along with being subsequently rolled out in every country in relation to their own realities.

Cancer pain has changed: multimorphism at the heart of the global analgesic strategy

If we want to highlight the elements of understanding and analysis, it is necessary to assume that cancer, its treatments, and cancer pain have changed in the last few decades. Today, when we mention cancer, we can schematically describe several types of situations, whether they are inaugural, evolutive, or recurring:

- cancer considered to be curative, the treatments for which are often combined and will make a cure possible;
- metastatic or chronic oligometastatic cancer, resulting in a chronic disease that requires complex, long-term therapeutic management;
- cancer with palliative evolution, for which the specific treatments are not sufficiently effective; this type of cancer can evolve more or less rapidly, depending on its aggressiveness;
- cured cancer, for which the sequelae can nevertheless have many chronic repercussions in terms of health, notably pain as a consequence of the disease and its treatments in cancer survivors.

By nature, pain may be present at all stages of the disease and even after cancer treatments. WHO recently modelled three types of care to classify the pathway for cancer patients [1]: “Supportive, survivorship and palliative care should be integrated into broader health services, with clear communication among different levels of care to improve overall outcomes and efficiency”. Without questioning these three entities, which have the merit of putting into place the context of care that we need to implement throughout the disease, regardless of how it evolves, we can consider these three entities as an integral part of supportive care [9]. “Supportive and survivorship care must be scaled up to promote treatment completion and reintegration into workplaces and communities. Palliative care must be a priority in all countries” [1].

In the face of these cancers, treatments have also benefited from major advances which have, for certain types of cancer, radically changed the prognosis of the disease by providing therapeutic precision: cancer surgery (with a wide range of mini-invasive approaches), radiotherapy (increasingly targeted with, for example, stereotaxis or proton therapy), chemotherapy, targeted therapies, immunotherapy, and hormonotherapy.

In parallel with this progress, cancer pain has also changed and become more complex: in a series of articles [6, 10–16], we described the concept of multimorphic cancer pain. “From an etymological point of view, the term multimorphic refers to the possibility of adopting several forms at the same time and of changing form. This term seems to us to be adapted to the dynamic definition that we have sought to give to cancer pain: this type of pain can effectively evolve in how it presents, in relation to the different factors, whether or not they are linked to cancer and its management. In short, cancer pain is not a fixed entity in itself or over time. It changes, alters, evolves, or devolves, presenting in different forms at any time, from the diagnosis until after the cure or in palliative situations when applicable. These modifications depend on a series of intrinsic or extrinsic factors generally associated with each other, which play a part in initiating an imbalance at the level of pain management and thus create disruptions. Today, many forms of cancer are seen as chronic conditions with varying degrees of improvement depending on type, considering cancer pain as multimorphic and managing it on the principle of the basics by preventing, identifying and treating these disruptions is a pertinent response to its complexity and the sustainability of the medical condition of these patients. Optimizing state of health and management of risk factors or comorbidities, promoting compliance and therapeutic education, for example are all factors that improve cancer pain management in particular, although not exclusively” [6].

This modelling is not purely intellectual. It is the fruit of the intersection between the scientific literature and our experiences as clinicians in the field. This interpretation makes possible up-to-date understanding of what cancer pain is today, that is, a complex nosological entity in its own right, capable of taking on a multitude of forms, and of changing throughout the care pathway, as well as an entity that requires an exhaustive approach that is not only based on the field of clinical practice.

A three-dimensional analgesic strategy (Fig. 1)

In a series of articles on multimorphic cancer pain, we proposed a strategy with four key points for optimizing the management of cancer pain [6]. In the present article, we present an updated and enhanced version of this strategy, in light of the latest guidelines. This new version integrates certain fundamental aspects that we thought it important to add (Fig. 1).

This three-dimensional strategy is based on:

- First dimension:

Fig. 1 Three-dimensional analgesic strategy

- An analgesic objective
- Three recommendations: prerequisites for managing cancer pain, identification of the elements that disrupt analgesic balance (Table 1), and an integrated, systemic model for supportive care in which these three dimensions must be found
- Second dimension: the care pathway starting from the cancer diagnosis, including the three types of care in comprehensive cancer care (supportive, survivorship, and palliative care)
- Third dimension: the key players involved, whose synergy and even interdependence will condition the success of the analgesic project. Patients are obviously the first key players (and experts in their own health), in association with healthcare professionals and the health system in which they find themselves, in the broadest sense of the term. This dimension has been added to our

Table 1 Criteria defining the multimorphic nature of cancer pain

Disruptions	Criteria defining the multimorphic nature of cancer pain		
Factors influencing the complexity of cancer pain	Components of the pain: <ul style="list-style-type: none"> ■ Nociceptive (includes inflammatory) ■ Neuropathic ■ Nociplastic* 	Aetiopathogenic mechanisms: <ul style="list-style-type: none"> ■ The cancer in itself ■ Its treatments (chemotherapies, targeted therapies, immunotherapies, hormone therapy, radiotherapy, surgery) ■ Other causes of pain 	Presentation of the pain: <ul style="list-style-type: none"> ■ Intensity ■ Duration of the pain (chronic, subacute, acute) ■ Background ■ Exacerbations/breakthrough pain ■ Pain emergencies
Intrinsic factors of variability over time concerning the cancer	Type of cancer and its stage on diagnosis	Progression of the disease including “chronic illness” cancer: <ul style="list-style-type: none"> ■ Cure ■ Sequelae ■ Relapse ■ Metastases ■ Palliative progression 	Evolution in the treatments and complications: <ul style="list-style-type: none"> ■ Cancer treatments ■ Supportive treatments ■ Complications
Extrinsic factors of variability over time concerning the state of health	Environmental factors: <ul style="list-style-type: none"> ■ Ethno-demographic factors/cultural and spiritual factors ■ Socio-economic/earliness/level of access to care/abandonment factors ■ Communication 	Inter-individual factors: <ul style="list-style-type: none"> ■ Genetics ■ Variability factors of pain thresholds ■ Immunity ■ Metabolism 	Intra-individual factors: <ul style="list-style-type: none"> ■ Motivation ■ Risk factors ■ Comorbidities/multi-morbidities ■ Intercurrent treatments ■ Treatment compliance ■ Treatment education

*The concept of nociplastic pain could be useful to explain complex syndromes in particular after cancer treatments, or when no link with the disease and its treatments is obvious: pain that (1) arises from altered nociception despite no (2) clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or (3) evidence for disease or lesion of the somatosensory system causing the pain (IASP Taxonomy 2017)

first model, indicating to what extent the success of the analgesic project is dependent on factors which, in most cases, go beyond the patients and even healthcare professionals themselves: the health environment is often the variable in the equation that can have the biggest impact on pain management because it integrates systemic aspects such as healthcare policies, the financial means made available (and thus, for example, access to treatments or the means dedicated to training), the legislation covering pain management, the degree of priority at the national scale, or even access to research, ethics, or new information and communication technology.

Discussion

Through these three dimensions, the management model that we propose must be able to cover every aspect of cancer pain in an exhaustive manner, including those beyond the purely clinical: even the very slightest negative point in this managerial approach can compromise optimal analgesic balance (Table 1). On the contrary, identifying these negative points makes it possible to optimize management. One notable point from the outset is the fact that the number of factors that work together to maintain satisfactory analgesic balance is significant and goes far beyond cancer pain in itself. In this sense, this model is innovative because it addresses other determinants that must be assessed at all costs, just as much as the more traditional aspects specific to pain that clinicians are used to assessing. In our opinion, it is only by integrating all these determinants that we can truly hope to improve the epidemiological figures for cancer pain in the long term.

Nevertheless, this model also highlights the fact that many of these factors can only be modified to a very small degree by healthcare professionals and even less by patients. If we question the statement in our title, cancer pain is over, if we want it, the answer risks being anything but simple. Yes, if we want it, we can always improve all the factors within our reach, in our roles as patients and healthcare providers. The lack of desire would necessarily be an obstacle. But we are limited by the determinants linked to our healthcare system, to the social and economic level of our country, or even to the desires—or absence thereof—that can range from the very smallest scale to those of a political nature. It is thus at the level of the third dimension (the healthcare system), that the “if you want it” takes on all its meaning. For comprehensive cancer care to be of the very highest quality, it must be effective, efficient, accessible, acceptable, as well as patient-centred, equitable, and safe [1]. The same is true for management of cancer pain. Initiatives such as the integrated missions of the Programme of Action for

Cancer Therapy (imPACT) provide both guidance and structure, allowing the member states to move towards a certain number of prerequisites and their assessment regarding implementation of plans to combat cancer [1]. Translating evidence into policies and programmes is a real challenge for managing cancer pain, a nosological entity whose existence has only very recently been accepted and which, by nature, branches into a wide variety of fields of medicine and healthcare.

Conclusion

The aim of the multidimensional approach that we adopt today regarding multimorphic cancer pain is to be exhaustive, through the continuum formed by the comprehensive cancer care pathway (Fig. 1). Managing cancer pain as the cornerstone of supportive medicine [6] can now be based on a solid modelled foundation to be implemented as much as possible in the field with our patients and healthcare providers.

One day, we hope to be able to say unconditionally, “cancer pain is over!”.

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