

Pain trajectories, progress and perspectives.

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Even after decades of investigation, the transition from acute pain to chronic pain is only partially understood (1). Surgery is a specific model to study this transition, combining programmed trauma, expected resolution and its correlate, a possible dysfunction leading to the transition to the chronic state (2). Interfering factors may exist, including a degree of vulnerability (related to the patient, i.e. medical history, comorbidities, genetics; but also iatrogenic factors, such as poor control of perioperative pain) with many open questions (such as the role of the specific means of preventing or treating pain, the role of opioids during and after surgery, the importance of patient education and the role of postoperative strategies) (3-8).

In this issue, L'Hermite *et al.* propose a pragmatic solution to interpret pain trajectories, which may be even more important in anticipating the risk of persistent pain than the pain scores themselves (9). They invited 344 patients and analyzed data from 308 patients, undergoing major general surgery, to perform a self-report of pain intensity during the first postoperative week. They observed that about one-third of patients had a "non-ideal pain trajectory" defined as "late, transient, or no relief" (i.e., a numerical rating scale, NRS > 4 after day 3), which was the primary endpoint. After three months, 31% (95% confidence interval, CI: 26 to 37) of patients presented with persistent post-surgical pain (PPSP) of varying presentation, severity and functional consequences. Among others, a "non-ideal" pain trajectory was the only independent postoperative risk factors of PPSP, with an odds ratio of 2.25; (95% CI: 1.26 to 4.01), $P = 0.006$]. The other risk factors were directly related to the preoperative chronic pain.

L'Hermite *et al.* confirm that a “non-ideal” pain trajectory remains a common reality, despite our best efforts. Their results are in line with others, showing that pain can remain a significant problem even when a maximized pain management protocol is introduced (10). And regarding the risk of pain persistence, their results confirm those of the PAIN OUT study, where the number of hours of severe pain was a greater risk factor than the worst pain score (11).

L'Hermite adds that if the pain trajectories are relevant, they should be followed for at least seven days, so often after discharge and generally outside the scope of the anaesthesiologist (2).

Of course, an association does not prove causation. Their study was not designed to prove that improving pain trajectories would actually reduce the incidence of PPSP. But for that, researchers need proof of concept studies, as they have done, and clinicians, a pragmatic interpretation, as offered here. Interestingly, they collected data on the various functional consequences of PPSP. These variations may suggest that a patient-centered and pain-specific approach might be the only valid option. Recent reports suggest, for example after breast cancer surgery, that pain is a complex phenomenon, a fragile endpoint, very fluctuating and perhaps more often musculoskeletal than neuropathic (Figure) (12). Unfortunately, L'Hermite *et al.* did not collect data on the occurrence of non-localized pain at the operative site, which could have been considered essential from a patient perspective. In other words, patients' perspective and functional goals must be integrated in a holistic way. This is of utmost importance because it has been suggested that when they do not focus solely on pain at the surgical site, the acute pain trajectories no longer correlate with PPSP. Moreover, this should

not be considered at one point in time, but rather over time, because even when considering neuropathic pain, the pain may go away and reappear later (12).

In conclusion, while we have not yet identified the optimal way to predict PSPP, important clues and proof of the feasibility of self-report data collection tools are important steps paving the way for future development, including through patient-centered approaches.

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Figure legend

Figure. Pain localisation trajectories between the first and the second postoperative year after breast cancer surgery (from [12] with permission)

Figure

