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## Reduction of breast cancer relapses with perioperative non-steroidal anti-inflammatory drugs: New findings and a review

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A bimodal pattern of hazard of relapse among early stage breast cancer patients has been identified in multiple databases. Using computer simulation and access to a very high quality database from Milan for patients treated with mastectomy only, we proposed that relapses within 3 years of surgery are stimulated somehow by the surgical procedure. Retrospective breast cancer data from a Brussels anesthesiology group suggested a plausible mechanism. Use of ketorolac, a common NSAID analgesic used before surgery was associated with far superior disease-free survival. The expected prominent early relapse events in months 9-18 are reduced 5-fold. Transient systemic inflammation accompanying surgery (identified by IL-6 in serum) could facilitate angiogenesis of dormant micrometastases and

proliferation of dormant single cells and could have been effectively blocked by the perioperative NSAID. If this observation holds up to further scrutiny, it could mean that the simple use of this safe, inexpensive and effective anti-inflammatory agent at surgery might eliminate early relapses and reduce mortality by 25 to 50%. This hypothesis has been recently confirmed in a mouse model by Krall et al in *Science Translational Medicine* 2018 and a second retrospective study by Desmedt et al in *JNCI* 2018. Post-operative bleeding is a major concern with perioperative NSAIDs however tranexamic acid has been found to reduce such bleeding by 39% in a clinical trial by Ausen et al in *BJ Surg* 2018.

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