

Yog anatomy: Educating and Inspiring



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What began as a spiritual practice in India's deep-rooted philosophy has become popular as a way of promoting physical and mental well-being. The beauty of yoga is that whether you are young or old, overweight or fit, it has the power to calm the mind and strengthen the body. Studies have suggested possible benefits of yoga for several aspects of wellness, including stress management, mental/emotional health, promoting

healthy eating/activity habits, sleep, and balance.

In this era of globalization where lifestyle and dietary food patterns are changing drastically, it is pertinent to explore and establish the interrelationship among various Indian traditional sciences to offer comprehensive and holistic healthcare. Tata Memorial Centre (TMC), Mumbai adopted yoga to design a study which is robust for a Western kind of testing. Patients were taken to upper echelons of understanding and practicing yoga which was done in three stages: breathing, asanas and spirituality.

The study on breast cancer was conducted among two sets of patients. One who received chemotherapy and yoga sessions before surgery and radiation whereas the other ones who started yoga and chemotherapy post surgery. The patients were evaluated for their physical strength, emotional stability, feeling of wellbeing, fatigue and whether



they were spiritually evolved in any way and did the survival improve. The yoga experts and caretakers of the patients tailormade the process in such a way that each of those stages would be easily possible to do at a time when they were going through treatment. The result was an improvement that was better compliance to the treatment. In addition, the patients were found extremely happy as far as their quality of life was concerned.

Prime Minister's recent 'Mann ki Baat' highlighted this effort by TMC which has made more and more people aware about the treatment. The yoga

sessions and details about the treatment will soon be available for free for individuals on the website of Tata Memorial Centre. This initiative has also encouraged schools to reach out and include yoga as a part of their curriculum.

The balance between effort and ease in yoga practice is a moving target. But, the more attention is given to the overall feel in the practice, the better it will be to identify whether the intensity of practice needs to go up or down. The more often a balance is made between effort and ease in our yoga practice, the more often yoga can be enjoyed and be benefitted from.

Peritumoral Lidocaine Injection: A Low-Cost, Easily Implemented Intervention to Improve Outcomes in Early-Stage Breast Cancer

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Improvements in breast imaging and the routine use of breast cancer screening have resulted in increased rates of breast cancer cases diagnosed at early stages of disease, before metastatic dissemination. Additionally, advances in local regional and systemic therapies have significantly decreased the likelihood that patients treated for early-stage disease will recur. Despite these advances, it is generally thought that up to 30% of women treated for early-stage breast cancer eventually develop metastatic disease, suggesting additional opportunities to identify effective interventions to prevent breast cancer recurrence. One opportunity that has not been studied extensively is to intervene in the immediate perioperative period.

Although conclusive clinical data are lacking, largely preclinical work has suggested that surgical excision of a tumor and the surgical stress response can induce metastasis (Fig 1). An evolving understanding of these mechanisms potentially driving recurrence after surgery, such as modification of immune function, activation of neural and proinflammatory signaling, dissemination of circulating tumor cells, and increasing prometastatic pathways, has created interest in studying the utility of anesthetic agents or strategies as a form of cancer therapy.¹⁻³ One such example, investigated in the trial by Badwe et al,⁴ is the use of lidocaine, an amide local anesthetic that blocks voltage-gated sodium channels, thereby decreasing pain by preventing the initiation and conduction of impulses along nerves. Alleviating pain may be an indirect effect on the spread of cancer by decreasing the surgical stress response. Preclinical data suggest that lidocaine may also have direct effects by altering pathways important for tumor cell proliferation, angiogenesis, and invasion and by promoting apoptosis.⁵⁻⁸

In the current study, Badwe et al⁴ randomly assigned patients with early breast cancer to peritumoral injection of 0.5% lidocaine, 7-10 minutes before surgery (lido-arm) or surgery without lidocaine (no lido arm). The trial's primary end point was disease-free survival (DFS) defined as time between random assignment and occurrence of local, regional, or distant recurrence of invasive breast cancer, the development of contralateral breast cancer, or death due to any cause. Early breast

cancer was defined as operable breast cancer with clinically node negative (cN0) disease or limited nodal disease (cN1) and no evidence of distant metastasis. Patients were eligible if undergoing surgery as their initial intervention regardless of disease subtype. There were 1,583 evaluable patients, including 786 in the lido arm and 797 in the no lido arm. The groups appear relatively well balanced, with 25.3% in the lido arm and 22.2% in the no lido arm having triple-negative breast cancer and 19.6% in the lido arm and 20.2% in the no lido arm having human epidermal growth factor receptor 2-positive (HER2+) breast cancer. Of note, only 35% of patients with HER2+ disease in both arms of the trial received HER2-targeted therapy. With respect to other risk factors, the groups were comparable with respect to the percentage of patients with grade III tumors (approximately 74%) and pathologically node-positive disease (45%). After a median follow-up of 68 months, 5-year DFS rates were 86.6% in the lido arm and 82.6% in the no lido arm (hazard ratio [HR], 0.74; 95% CI, 0.58 to 0.95; $P = .017$). Importantly, the majority of events were breast cancer-related. In the lido arm, 73.6% (70 of 95) were distant recurrences and 20.0% (19 of 95) were locoregional. In the no lido arm, 75.2% (94 of 125) of the events were distant recurrences and 17.6% (22 of 1,125) were locoregional. Contralateral breast cancer or the development of a non-breast primary cancer occurred in 6.3% (6 of 95) of the lido arm and 7.2% (9 of 125) of the no lido arm. The 5-year overall survival (OS) rates were 90.1% and 86.4% in the lido and no lido arms, respectively (HR, 0.71; 95% CI, 0.53 to 0.94; $P = .019$).

It is noted that because of slow accrual and fewer than anticipated DFS events, the trial's statistical plan was revised from powering the study to detect a 7.0% absolute improvement in the lidocaine arm and, assuming a 60.0% 5-year DFS rate in the control arm, an HR of 0.784, to powering the study to detect an absolute 6.0% DFS increase in the lidocaine arm and, assuming a 5-year DFS rate of 80.0% in the control arm, an HR of 0.676. This 6.0% DFS benefit was felt to be clinically relevant. The trial did not see that benefit, therefore was technically a negative study. However, it is hard to suggest that the 4.0% DFS benefit (and 3.7% OS benefit) that was seen is not clinically significant,

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THE TAKEAWAY

In the article that accompanies this editorial, Badwe et al⁴ show that peritumoral injection of lidocaine before surgery leads to improvements in disease-free survival and overall survival in patients with early-stage breast cancer. These findings support the use of peritumoral lidocaine as a low-cost intervention that can be easily implemented into the care of patients with breast cancer.

particularly given the ease of the intervention and the lack of any adverse events attributable to the lidocaine injection.

The mechanisms by which benefit was achieved through lidocaine administration are not clear, as acknowledged by the study's authors. It is interesting to compare the results of this study with another randomized controlled trial by Sessler et al⁹ that compared the rates of breast cancer recurrence in patients receiving regional anesthesia with paravertebral blocks and propofol with those receiving general anesthesia with sevoflurane and opioid analgesia.

The hypothesis those investigators sought to test was that regional anesthesia, which eliminates the surgical stress response as well as the use of volatile anesthetic agents and opioids for anesthesia, would result in lower breast cancer recurrence rates. The agent used in the paravertebral block was ropivacaine, a long-acting amide local anesthetic.¹⁰ The trial randomly assigned 2,108 patients and after a median follow-up of 36 months, the recurrence rate in both groups was 10% (HR, 0.97; 95% CI, 0.74 to 1.28; *P* = .84). The differences in the results of these two trials, one using a

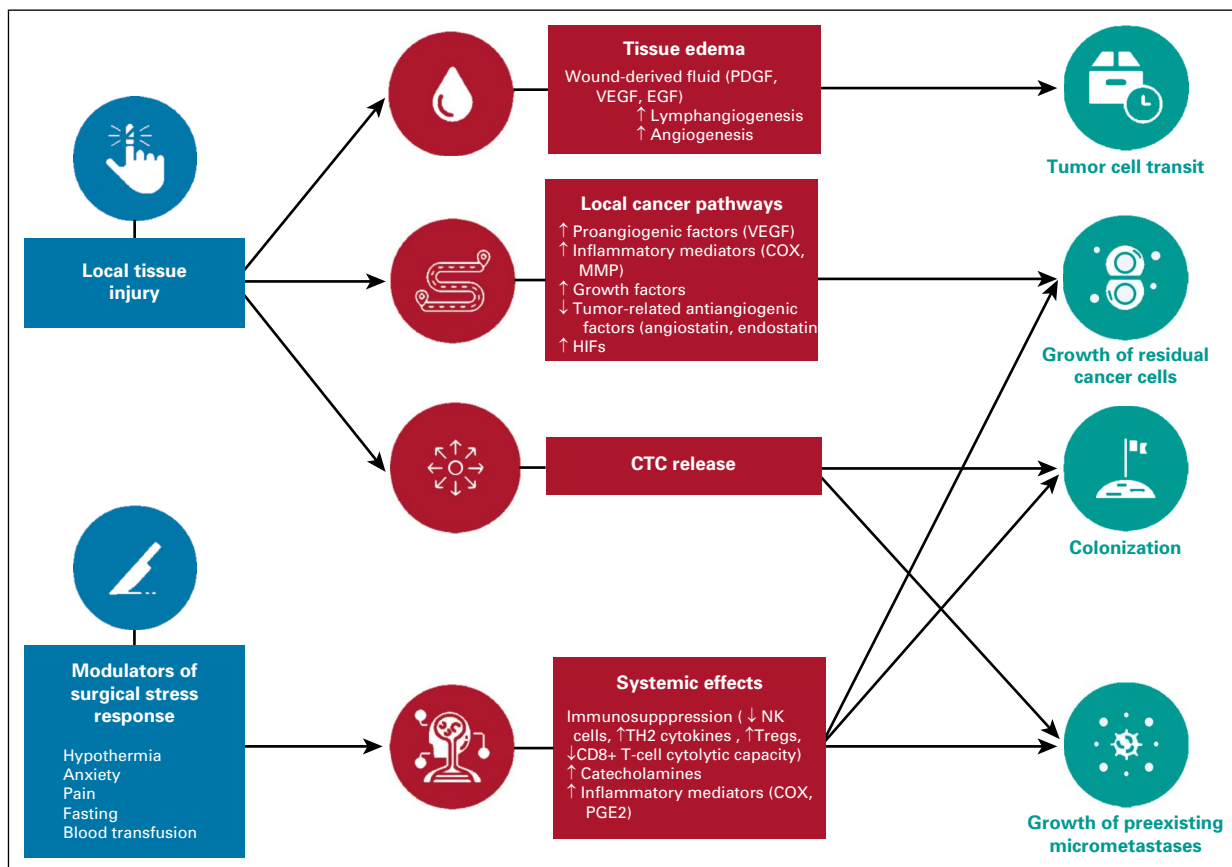


FIG 1. Perioperative drivers of cancer recurrence. Multiple mechanisms attributable to local tissue injury and the surgical stress response have been proposed as promoting cancer recurrence after surgery. COX, cyclooxygenase; CTC, circulating tumor cell; EGF, epidermal growth factor; HIF, hypoxia-inducible factor; MMP, matrix metalloproteinases; NK, natural killer; PDGF, platelet-derived growth factor; PGE2, prostaglandin E2; TH2, T-helper 2; Tregs, regulatory T cells; VEGF, vascular endothelial growth factor. Adapted from Hiller JG, Perry NJ, Poulogiannis G, et al, "Perioperative Events Influence Cancer Recurrence Risk After Surgery," *Nature Reviews Clinical Oncology*, 15, 205-218, 2018, Springer Nature.¹

local anesthetic as a component of a paravertebral block and the other injecting the local anesthetic directly into the tissue, may lead one to hypothesize that the benefit of lidocaine is due in part to its modulation of the effects of local tissue injury induced by surgery. Counter to that hypothesis is the observation that patients on the current study benefitted whether they underwent lumpectomy, in which case the tissue surrounding the tumor was maintained or mastectomy, in which case the entire breast, including the tumor and surrounding tissue, was removed. Mastectomy was performed in 37.3% of patients on the study, and the forest plot for DFS showed an HR of 0.72 (95% CI, 0.50 to 1.04). This numerical trend favored administration of lidocaine; however, it was not statistically significant. The HR for OS for mastectomy patients was 0.62 (95% CI, 0.42 to 0.92), strongly favoring administration of lidocaine.

With the mechanism by which lidocaine resulted in improved DFS and OS being unclear and the fairly striking difference in outcomes between the arms of the trial, it makes one question the study results and whether the results are applicable to their clinical practice. One could rightly suggest that the patients do not necessarily resemble those cared for in their practice, particularly with a high percentage of HER2+ patients not receiving HER2-targeted therapy and a high percentage of patients undergoing axillary lymph node dissection, including patients with pathologically node-negative disease. The trial only enrolled patients undergoing up-front surgery, and in current practice, the majority of patients with HER2+ and triple-negative breast cancer receive preoperative systemic therapy. However, it was a large, multicenter, randomized trial, suggesting generalizability of the results. And the results of the study are interesting, particularly as we consider other therapeutics

used in the treatment of patients with breast cancer. The administration of peritumoral lidocaine before surgery resulted in a 4.0% DFS benefit at 5 years which is not that dissimilar from benefit we see from many systemic therapies that carry potential toxicity risk. On the basis of the recently reported 8-year follow-up of the APHINITY trial, pertuzumab is administered in the adjuvant setting for patients with HER2+ breast cancer for a 2.6% invasive DFS benefit.¹¹ On the basis of 4-year follow-up data from the monarchE trial, abemaciclib is administered adjuvantly to patients with high-risk hormone receptor-positive breast cancer for a 6.4% invasive DFS benefit.¹² And on the basis of the KEYNOTE-522 study, pembrolizumab is administered in the neoadjuvant setting, continued adjuvantly for patients with triple-negative breast cancer for an approximately 7% event-free survival benefit at 3 years.¹³

In summary, peritumoral injection of 0.5% lidocaine before surgery offered a clinically meaningful improvement in DFS and OS with relative risk reductions of 26% and 29%, respectively, compared with no lidocaine administration. These data add to the body of evidence supporting the perioperative use of local anesthetics for multiple reasons to include not just this potential oncologic benefit but for providing pain relief, as well as decreasing intraoperative and postoperative opioid use, thereby reducing postoperative nausea and vomiting and facilitating enhanced recovery after surgery.¹⁴ As concluded by the study investigators, it seems reasonable to introduce this intervention as an easy, cost-effective intervention that may reduce the rates of recurrence and death in women with early-stage breast cancer. Additional investigation will be required to elucidate the mechanism of this benefit.

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