Perioperative Protocols

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Peri-operative Pain

Protocol Modifications

Modifications for non-Orthopedic surgery and Non-Chronic Opioid Management

The core nutraceutical perioperative management protocol from the 4-D framework does not require major changes for non-orthopedic surgery or for chronic pain patients not on long-term opioid therapy. The four pathogenic domains (Systemic Inflammation, Neuroinflammation, Oxidative Stress, Mitochondrial Dysfunction) and the perioperative biology they target are independent from the types of surgery — these domains impact patients across all surgical specialties. However, there are several **procedure-specific and patient-specific modifications** worth incorporating.

Modifications That Are Procedure-Specific

1. Gastrointestinal (GI) Surgery

NSAID Considerations The most significant difference for GI procedures surrounds surgery with intestinal anastomosis (sewing or stapling two healthy ends of the bowel together after a diseased section is removed). NSAIDs (Non-Steroidal Anti-inflammatory Drugs - especially diclofenac) may be associated with increased anastomotic leak risk.This means that when NSAIDs are restricted or avoided in GI surgery, the opioid-sparing role of the 4-D nutraceutical panel becomes even more important.

Specifically:

- **Omega-3 (EPA/DHA)** continuation through surgery gains additional importance as an anti-inflammatory agent that does not carry anastomotic leak risk and supports inflammation resolution.
- **PEA (palmitoylethanolamide)** continuation provides anti-neuroinflammatory effects without increased anastomotic leak risk.
- **Magnesium** (oral and IV) provides independent opioid-sparing effects.

Antioxidant-Enriched Nutrition Antioxidant-enriched tube feeding after major GI surgery reduces inflammation.This supports the continuation of the 4-D Protocol's antioxidant-targeting nutraceuticals in the postoperative period for GI patients, with the same phased restart protocol used for orthopedic patients..

Specifically:

- **NAC**
- **Alpha-lipoic acid**
- **CoQ10**

2. Gynecological Surgery: No Major Protocol Differences

For gynecological procedures, the perioperative nutraceutical protocol is essentially identical to the orthopedic framework. The same bleeding-risk considerations apply for the "hold" group (curcumin, resveratrol, quercetin, boswellia, sulforaphane). One consideration: quercetin should be avoided in patients with estrogen-dependent cancers,.

3. The "Continue/Hold" Framework Remains Unchanged Across Surgery Types

Based on their potential for contributing to perioperative bleeding, nutraceuticals may still need to be put on temporary hold for minor gynecological or GI endoscopic procedures. The consequences of a patient continuing a "hold" supplement are less concerning than for major orthopedic surgery. (See below)

Modifications That Are Patient-Specific

Opioid-Naïve vs. Opioid-Tolerant)

For chronic pain patients **not on long-term opioid therapy**, the nutraceutical protocol itself does not change — the same 4-domain profiling drives nutraceutical selection regardless of opioid status.

However, the clinical context shifts:

- **The urgency of multimodal non-opioid strategies** is somewhat reduced because opioid tolerance, OIH, and withdrawal are not factors. The nutraceuticals still serve their domain-specific roles (anti-inflammatory, anti-neuroinflammatory, antioxidant, mitochondrial support), but the pressure to maximize every non-opioid analgesic pathway is less acute.
- **Melatonin** may warrant particular emphasis in opioid-naïve patients. A 2026 meta-analysis of 23 RCTs (2,028 patients) found melatonin was superior to placebo for postoperative pain, with effects comparable to active analgesic controls, and a separate RCT demonstrated 50% reduction in subjective pain perception in early postoperative days with prophylactic melatonin. For opioid-naïve patients where the goal is to minimize any opioid initiation, melatonin's anxiolytic and analgesic properties provide additional value.

3. The "Continue/Hold" Framework Remains Unchanged Across Patient Types

Based on their potential for contributing to perioperative bleeding, nutraceuticals may still need to be put on temporary hold for minor procedures. The consequences of a patient continuing a "hold" supplement are likely less concerning than for major orthopedic or spine surgery.

Supplements CONTINUED through surgery (applicable to all surgery types):

- Omega-3 (EPA/DHA) — Experts explicitly recommends continuation
- Magnesium glycinate
- Melatonin
- Vitamin D3 B-complex vitamins (including B12 & P5P)
- PEA
- Taurine
- Agmatine
- D-Ribose

Supplements HELD 2 weeks preoperatively (applicable to ***all*** surgery types)

Supplements with potential to interfere with blood clotting:

- Curcumin/turmeric
- Resveratrol
- Quercetin - additional caution in estrogen-dependent cancers
- Boswellia
- Sulforaphane
- CoQ10
- Alpha-lipoic Acid (cardiovascular/metabolic considerations).
- NAC — hold 24 hours only.

A procedure-specific nuance for the "hold" group

Risk differs by procedure — for procedures where bleeding would be particularly dangerous (intracranial surgery, spine fusion), strict adherence to the hold protocol is essential, whereas for lower-risk procedures, cautiously proceeding if a patient has not discontinued a supplement is reasonable. This means that for minor procedures such as endoscopies, the consequences of continuing a "hold" supplement are less concerning than for major surgery.