Enhanced recovery after surgery for primary hip and knee arthroplasty: a review of the evidence

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Abstract

Enhanced recovery after surgery (ERAS) protocols produce significant clinical and economic benefits in a range of surgical subspecialties. There is a long tradition of applying clinical pathways to the perioperative care of joint arthroplasty patients. Enhanced recovery after surgery represents the next step in the evolution of standardized care. To date, reports of full ERAS pathways for hip or knee arthroplasty are lacking. In this narrative review, we present the evidence base that can be usefully applied to constructing ERAS pathways for hip or knee arthroplasty. The history and rationale for applying ERAS to joint arthroplasty are explained. Evidence demonstrates improved outcomes after joint arthroplasty when a standardized approach to care is implemented. The efficacy of individual ERAS components in hip or knee replacement is considered, including preoperative education, intraoperative anaesthetic techniques, postoperative analgesia, and early mobilization after joint arthroplasty. Interventions lacking high-quality evidence are identified, together with recommendations for future research. Based on currently available evidence, we present a model ERAS pathway that can be applied to perioperative care of patients undergoing hip or knee arthroplasty.

Key words: arthroplasty; hip; knee; replacement

Enhanced recovery after surgery (ERAS) is rapidly becoming familiar to anaesthetists. Perioperative programmes incorporating multimodal, evidence-based interventions have come to be known as fast-track or ERAS pathways. Enhanced recovery after surgery was pioneered by Henrik Kehlet in the 1990s as an effort to improve recovery after colorectal surgery.1 Kehlet hypothesized that surgical stress, metabolic and endocrine derangements, and prolonged immobilization contribute to ‘organ dysfunction’: pain, nausea, vomiting, ileus, fatigue, and cognitive disturbance. The extent of organ dysfunction thus determines recovery. According to ERAS concepts, it is unlikely that any single surgical technique, anaesthetic intervention, or medication can significantly reduce organ dysfunction. Rather, recovery is facilitated by a multimodal approach directed towards global modulation of the surgical stress response. Enhanced recovery after surgery in colorectal surgery has consistently been associated with superior recovery, decreased morbidity, reduced hospital length of stay, and cost savings.2 The clinical and economic gains that can be achieved with ERAS have been demonstrated across a range of surgical specialties, including gynaecological oncology, urology, vascular, and thoracic surgery.3

According to the ERAS Society, there are ~20 components of care that influence the stress response and enhance recovery. It can quickly be appreciated that designing and implementing an ERAS protocol is a multidisciplinary endeavour. Accordingly, an ERAS team should comprise expertise from surgery, anaesthesia, nursing, physical therapy, and nutrition. The team has primary responsibility for reviewing the available literature and for formulating and delivering the protocol. Once implemented, a key plank in any ERAS platform is audit, with continuous evaluation of component efficacy and institutional compliance (Fig. 1).
Confusion exists about what constitutes ERAS vs other pathways of clinical care (Table 1). There is no internationally accepted definition of what constitutes a clinical pathway. Like ERAS, clinical pathways ensure an evidence-based set of patient orders and interventions, so that the most important elements of care are consistently delivered. It is the inclusion of audit that most distinguishes an ERAS protocol from a clinical pathway. Enhanced recovery after surgery mandates collection and analysis of outcomes and compliance. Enhanced recovery after surgery also stresses refining components of the pathway based on evolving evidence. In this way, ERAS can be viewed not only as a package of evidence-based interventions, but also as a process to facilitate consensus and research.

**Outcomes in orthopaedic surgery**

Despite widespread success in multiple surgical subspecialties, ERAS remains formally understudied and under-reported in the orthopaedic surgery literature. Nonetheless, there is persuasive evidence that ERAS concepts can also be applied to orthopaedic surgery, particularly elective hip and knee arthroplasty. In one of the earliest examples, Sharrock and colleagues applied a bundle of interventions to patients undergoing hip or knee replacement: epidural anaesthesia replaced general anaesthesia, invasive haemodynamic monitors became routine, high-risk patients received postoperative intensive care monitoring, postoperative epidural analgesia was used, pulse oximetry was introduced, and postoperative patients routinely received supplemental oxygen. Although no changes were reported in surgical technique, the mortality rate for total knee arthroplasty decreased from 0.44 to 0.07%.

Sharrock’s work can be viewed as an early model for ERAS in orthopaedic surgery. A more recent precursor of ERAS for joint arthroplasty was the development of clinical pathways. Although no two pathways are the same, each includes a range of pre-, intra-, and postoperative components and interventions. Chief among these are preoperative patient education, provision of adequate multimodal analgesia, and early mobilization after surgery. A significant body of work on the efficacy of joint arthroplasty pathways has been published by Hebl and colleagues at the Mayo Clinic. The Mayo Clinic’s Total Joint Regional Anesthesia Clinical Pathway includes regional anaesthesia techniques (peripheral nerve blocks and catheters), pre-emptive analgesia, and postoperative opioid-sparing multimodal analgesia. Patients who have surgery on the pathway experience superior analgesia, fewer opioid-related side-effects, fewer postoperative complications, shorter length of stay, and greater cost savings.

A major limitation to comparing the effectiveness of one clinical pathway with another is that a pathway is not a standardized intervention. Accordingly, comparative research has focused on the concept of pathways, rather than the components themselves. A systematic review of clinical pathways used in joint replacement surgery included 22 studies totalling...
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**Evidence to support individual ERAS components in total joint arthroplasty**

Studies implementing ERAS pathways for joint replacement in totality are sparse. However, individual components of typical ERAS protocols have been investigated separately. The remainder of this review summarizes the current state of knowledge regarding components that are classically included in ERAS protocols and that can be applied usefully to total joint arthroplasty. For many clinical choices controversy reigns, but creation of an ERAS programme necessitates making a series of difficult choices in the face of uncertainty. In this article, we attempt to present major areas of disagreement and suggest reasonable ways forward. Future audit and research could profitably investigate ERAS protocols for joint arthroplasty based on these components, both to document outcomes and to refine the choice of components.

**Preoperative education and counselling**

Anticipation of surgery can lead to anxiety and fear for many patients. An early study found that explicit pre-anaesthesia education significantly relieved anxiety and emotional stress before hip or knee replacement. Preoperative education contributes to higher patient confidence, greater patient satisfaction, and early recovery and discharge. It is essential that a preoperative education programme should establish achievable goals for postoperative oral intake, analgesia, physical therapy, and mobilization.

**Preoperative fasting and carbohydrate loading**

Enhanced recovery after surgery has challenged the time-honoured tradition of fasting from midnight to avoid pulmonary aspiration during elective surgery. Several systematic reviews found no evidence to support a safety benefit of prolonged fasting. Enhanced recovery after surgery consensus guidelines now permit intake of clear fluids until 2 h before induction of anaesthesia and a 6 h fast for solid foods. The safety of a
2 h-clear/6 h-solids fast is also upheld in obese and morbidly obese cohorts,30 and in patients with uncomplicated diabetes mellitus.31 A more conservative fast is recommended for diabetic patients with gastroparesis.32 In addition to liberalized fasting guidelines, ERAS protocols recommend that patients consume up to 300 ml of a clear carbohydrate-rich drink 2–3 h before surgery, with the goal of presenting the patient for surgery in a metabolically ‘fed’ state.33 A patient in an anabolic state undergoes less postoperative nitrogen and protein loss38 and maintains more lean muscle mass.34 These concepts are supported by several randomized controlled trials, indicating accelerated recovery after colorectal surgery when patients receive preoperative carbohydrate loading.35 36

There are limited data specifically exploring the role of metabolic state and recovery after joint arthroplasty. In a recent pilot study, 32 patients undergoing primary hip arthroplasty were randomized to usual care or a package of nutritional interventions, including preoperative supplementation and carbohydrate drink.57 Length of hospital stay and C-reactive protein were both significantly reduced in the intervention arm. There were no differences in complications between the groups. Another study randomized 29 patients to carbohydrate-rich drink 2 h before primary hip arthroplasty vs no beverage.58 The primary outcome was metabolic state, as determined by insulin-like growth factor-1 concentrations. Compared with placebo, patients who received the carbohydrate beverage had significantly higher insulin-like growth factor-1 at 5 days and 2 months after surgery, which was interpreted as evidence of anabolic status. Higher insulin-like growth factor-1 did not translate into long-term changes in body composition. There was a trend toward more fat loss in patients who underwent surgery later in the day, ostensibly because of prolonged fasting and catabolic state.

Others have argued that it is not the carbohydrate content of the beverage that confers a protective benefit, but the volume status of the patient at the time of induction of anaesthesia.59 To test this, 66 patients were randomized to fasting, water, or a carbohydrate drink before total hip arthroplasty under spinal anaesthesia. There were no differences between the three groups in any markers of catabolism (insulin resistance, glucose clearance, or cortisol concentrations) or haemodynamic status. However, patients in the fasting group received 10% more intraoperative i.v. colloids.

Taken together, there are currently insufficient data to make a decision for or against preoperative carbohydrate supplementation for joint arthroplasty. It is unclear whether supplementation contributes to (i) a metabolically fed state during surgery, and (ii) whether that state contributes to improved outcomes. The available evidence is from small trials of hip arthroplasty patients. The methods used for assessing anabolic/catabolic state are inconsistent and not without controversy.59 However, the risk vs benefit of liberal fasting and carbohydrate loading before elective colorectal surgery suggests that similar concepts could be applied safely and effectively to elective joint replacement.

### Standardized anaesthetic protocol

There is a physiological argument that regional anaesthesia is the optimal ERAS technique for hip and knee replacement. Neuraxial anaesthesia is sufficient for surgery, provides a sympathetic block, inhibits stress hormone release, and attenuates postoperative insulin release.40 41 A body of evidence demonstrates a higher incidence of postoperative complications when primary hip or knee arthroplasty is performed under general compared with neuraxial/regional anaesthesia. Pulmonary compromise, pulmonary embolus, need for transfusion, renal injury, infection, length of stay, and 30 day mortality are all significantly lower after neuraxial anaesthesia.42–44 Others suggest that outcomes are equivalent between techniques.45 46 These results are difficult to reconcile because there are multiple sources of potential bias. Registry-based data are subject to selection bias, and older, outdated modes of general anaesthesia could contribute to the appearance of neuraxial superiority. In contrast, randomized controlled trials (and the resultant meta-analyses) have their own sources of bias, including difficulty in generalizing results from (often) healthy study subjects to the much less selected patients found in everyday clinical practice.

A recent study comparing total i.v. anaesthesia vs spinal anaesthesia for total knee arthroplasty found a 6 h reduction in length of stay and less nausea, dizziness, and orthostatic instability in the total i.v. anaesthesia group.47 This study has been criticized for suboptimal analgesic design of the neuraxial group.48 Reduced length of hospital stay is otherwise consistently associated with the use of a neuraxial compared with a general anaesthetic. The most recent meta-analysis of 29 studies, including 10 488 patients, showed that neuraxial anaesthesia reduces length of stay by almost half a day compared with general anaesthesia.49 Multi-institutional retrospective studies associated the use of general anaesthesia with an 8.5-fold increased risk of moderate to severe postoperative pain49 and a 2.5-fold increased risk of persistent postsurgical pain, for hip and knee arthroplasty.50 These data provide additional motivation to use neuraxial anaesthesia.

### Preventing and treating postoperative nausea and vomiting

Postoperative nausea and vomiting (PONV) can be more distressing than pain.51 Risk factors include female sex, non-smoking status, a history of motion sickness or previous PONV, and predicted requirement for postoperative opioids.52 The best way to manage PONV is probably to avoid general anaesthesia and to minimize opioids, as discussed elsewhere in this review. Based on the criteria of Apfel and colleagues,52 patients at moderate risk of PONV (i.e. two risk factors) should receive prophylaxis with dexamethasone at induction or a serotonin receptor antagonist at the end of surgery. High-risk individuals (three or more factors) should receive both dexamethasone at the beginning of surgery and a serotonin receptor antagonist at the end of surgery.

Forsaking dexamethasone prophylaxis in a diabetic patient should be decided on an individual basis, after balancing the individual risk of PONV with hyperglycaemia. Dexamethasone increases blood glucose in both diabetic and non-diabetic patients in a dose-dependent fashion, but evidence of an association with complications is currently lacking.53 54 Furthermore, the peak hyperglycaemia is limited in diabetic patients and can probably be managed effectively with perioperative insulin.55

### Postoperative analgesia

Enhanced recovery after surgery protocols advocate multimodal, opioid-sparing techniques as the basis for postoperative pain control.29 For this reason, use of epidural analgesia,
The role of additional oral adjuvants for multimodal analgesia is unclear. A meta-analysis found opioid sparing from gabapentin for knee arthroplasty. The anticonvulsant pregabalin has been studied, with mixed evidence that perioperative pregabalin reduces opioid consumption and prevents chronic neuropathic pain after total knee or hip arthroplasty. However, in conjunction with an epidural, adductor canal block, and multimodal oral analgesia after knee arthroplasty, pregabalin was associated with increased sedation, lower patient satisfaction, and no benefit on pain scores. There is recent interest in gabapentinoids as adjuncts to prevent PONV after joint arthroplasty by virtue of the opioid-sparing effect. Some meta-analyses show that gabapentinoids reduce nausea after hip or knee replacement, although there was no effect on the incidence of vomiting in either study. Another meta-analysis failed to find any protective PONV effect of gabapentin after knee arthroplasty. These benefits need to be balanced against the risk of sedation or dizziness from gabapentinoids.

The antidepressant duloxetine, when added to a comprehensive postoperative analgesic regimen, also failed to affect pain scores after knee arthroplasty. However, duloxetine substantially reduced both opioid use and nausea. It is possible that the baseline analgesic regimen used in these latter two studies was so effective that the benefits of duloxetine and pregabalin were not revealed; future studies in institutions that do not use comprehensive multimodal pain therapy regimens may provide insight.

**Early mobilization**

Early mobilization is a key component of ERAS programmes. Adverse physiological effects of prolonged bed rest include increased insulin resistance, myopathy, reduced pulmonary function, impaired tissue oxygenation, and increased risk of thromboembolism. Safe and effective analgesia is a prerequisite to encourage postoperative mobilization. There is good evidence that early mobilization facilitates recovery after hip and knee arthroplasty. A recent meta-analysis shows a significant reduction in length of stay (by 1.8 days) when patients ambulate within 24 h of surgery. Early mobilization after knee arthroplasty is also associated with improved functional recovery and lower incidence of DVT.

Despite these benefits, it is unknown whether early mobilization is associated with other complications after joint arthroplasty, including loosening, dislocation, and bleeding. High-quality studies of postdischarge rehabilitation are also lacking, including the ideal composition and duration of a course of treatment.

**Maintaining normothermia**

Multiple series suggest that normothermia should be targeted as part of the anaesthetic care of the joint arthroplasty patient. Maintaining perioperative normothermia with forced-air heating has been firmly established to reduce infection, cardiac complications, coagulopathy, and transfusion requirements. Aggressive warming reduced intraoperative blood loss during total hip arthroplasty and was associated with reduced opioid need and greater satisfaction after total knee arthroplasty. Active intraoperative warming before tourniquet deflation prevented subsequent hypothermia in elderly patients undergoing primary knee replacement under general anaesthesia. Prewarming the operating room before total hip or knee replacement has been associated with improved postoperative outcomes, reduced blood loss, and decreased analgesic use.
replacement seems to be a less effective strategy and did not prevent intraoperative hypothermia in hip or knee replacement.102

One argument against maintaining normothermia is the possible neuroprotective effect of mild hypothermia. Short-term postoperative cognitive impairment has been associated with warmer temperatures in elderly patients after knee replacement.103 The long-term effects of mild hypothermia for joint replacement, who might benefit, and how to risk stratify patients are intriguing avenues for research. In the interim, there are sufficiently described benefits of normothermia to recommend a normothermic goal as part of ERAS protocols.

**Antimicrobial prophylaxis**

Infection after joint arthroplasty is a serious complication that can be difficult to treat.104 There is currently no defined guideline for antibiotic/antisepptic prophylaxis for joint replacement.105 The Agency for Healthcare Research and Quality-recommended regimen for patients undergoing primary hip and knee arthroplasty is cefazolin.106 Clindamyacin and vancomycin should be reserved as alternative agents, if there is a cephalosporin allergy or surveillance data indicating causative organisms. Intranasal mupirocin is recommended for all patients with documented S. aureus colonization.

Recent evidence from a large systematic review and meta-analysis indicated that systemic antibiotic prophylaxis before hip replacement significantly reduced the incidence of infection.107 For all other outcomes, including infection after knee replacement, there were no differences found in any comparisons made, including timing, route of administration, or dose of antibiotic studied. Overall, the quality of data was considered poor, with unclear or high risk of bias, and the majority of the studies (20 out of 30) were >20 yr old; importantly, patient characteristics, selection, optimization, and surgical and anaesthetic techniques have changed dramatically during this time. The authors end with a call to replicate some of the trials using large registries and taking into account local resistance patterns. They consider this especially important in primary knee arthroplasty, where no historic placebo comparator trials exist.

Antibiotic-loaded bone cement might reduce infection rates after joint arthroplasty. The evidence is more robust in hip compared with knee arthroplasty.107,108 A recent systematic review and meta-analysis concluded that there is a paucity of well-conducted trials, and evidence of the protective effect is insufficient to recommend routine use in primary knee replacement.109 Additional research into the role of antibiotic-loaded bone cement should also address concerns about patient safety, risk of antibiotic-resistant microorganisms, and increased cost.

**Intravenous fluid therapy**

Goal-directed fluid therapy (GDFT) is a prominent component of ERAS protocols in multiple surgical specialties.29 However, in contrast to colorectal surgery, GDFT might be less important for elective joint replacement. Blood and fluid losses are likely to be low, and the chance of early oral intake likely to be high. Thus, intraoperative fluid regimens can be more restrictive for hip or knee replacement. In any event, there are limited data exploring GDFT in hip or knee replacement. A recent trial randomized 120 patients to no-protocol (control, n = 40), conservative (n = 40), or GDFT using a non-invasive arterial pressure monitoring device based on pulse pressure variation.110 Results were significant for reduced postoperative infection, organ complications, and risk of blood transfusion in the GDFT group compared with control. Unlike other surgical subspecialties, in elective joint replacement the role, type, and volume of i.v. fluids have not been investigated. The effects of i.v. fluid on postsurgical outcomes are likewise unknown. These topics are ripe for future investigation.

**Blood conservation**

A conservative blood management strategy is crucial to the success of an ERAS programme. Allogeneic blood transfusion is associated with immunomodulation and volume overload.111,112 On the contrary, transfusion and anemia are both associated with increased incidence of infection, increased length of stay, and higher mortality after joint arthroplasty.111–113 Risk factors associated with allogeneic transfusion after knee replacement include age >75 yr, male sex, hypertension, and BMI <27 kg m².114,115 The presence of more than one risk factor significantly increases the likelihood of transfusion, suggesting that correction of preoperative anemia is particularly important in patients with multiple risk factors.116 Options to increase preoperative haemoglobin include iron supplements117 and erythropoietin.118 Both are associated with a lower requirement for transfusion after hip and knee arthroplasty.

There are several strategies for intraoperative blood conservation. Hypotensive epidural anaesthesia for primary hip arthroplasty minimizes blood loss119 without increasing complications, including stroke and myocardial infarction,120 or renal injury.121 Blood salvage techniques minimize the effects of acute blood loss during both total hip122–124 and total knee arthroplasty.125–127 However, blood salvage did not eliminate the need for allogeneic transfusion, especially in patients with low preoperative haemoglobin. Pharmacological interventions—specifically, the antifibrinolytic tranexamic acid—have supplanted cell salvage techniques in recent years,128 with multiple publications demonstrating both clinical and cost efficacy in hip,129,130 knee,131–133 and bilateral total knee arthroplasty.134 Tranexamic acid reduces blood loss and the risk of transfusion irrespective of the route of administration (i.v.135 or topical).136 The benefits afforded by tranexamic acid are achieved without significant increase in side-effects, including DVT, PE, stroke, myocardial infarction, or seizure.131,133,137

**Venous thromboembolism prophylaxis**

Current guidelines from the American College of Chest Physicians (ACCP) recommend routine use of anticoagulants to prevent clinical and radiographic DVT and PE after joint arthroplasty.138 Choices reviewed in the most recent guidelines include low-molecular-weight heparin (LMWH), a direct oral anticoagulant (DOAC; either a direct thrombin inhibitor or factor Xa inhibitor), low-dose unfractionated heparin, a vitamin K antagonist (usually warfarin), aspirin, and an intermittent pneumatic compression device. The minimal recommended duration of thromboprophylaxis is 10–14 days; however, the ACCP guidelines now suggest this could be extended up to 35 days.138

An alternative view, promulgated by the American Academy of Orthopaedic Surgeons, is that the ACCP guidelines focus inappropriately on prophylaxis that is effective for prevention of DVT, as a surrogate for PE.139 The American Academy of Orthopaedic Surgeons considers symptomatic PE, fatal PE, or
death as the primary outcomes of importance after hip or knee replacement. Some authors have criticised the premise that venographic evidence of DVT is equivalent to symptomatic, fatal PE, because there does not appear to be a direct correlation between DVT and PE. For example, DVT is two- to three-fold more common after knee replacement compared with hip replacement, yet total knee arthroplasty is associated with a reduced incidence of PE, compared with total hip arthroplasty. Additionally, all-cause mortality is higher in patients taking potent anticoagulants (LMWH or DOAC) than in patients receiving aspirin or warfarin, and clinically significant PE occurred despite the use of anticoagulants.

Other data suggest that DOACs might be superior to LMWH after hip or knee arthroplasty. For example, RECORD (Regulation of Coagulation in Orthopaedic surgery to prevent Deep vein thrombosis and pulmonary embolism) consisted of four double-blind, randomized studies comparing oral rivaroxaban (factor Xa inhibitor) with LMWH. Two studies were performed in patients undergoing total hip arthroplasty and two in total knee arthroplasty. A pooled analysis of all four studies found that rivaroxaban reduced the primary composite end point of venous thromboembolism (VTE) and all-cause mortality, although the majority of the effect was via a reduction in asymptomatic VTE. There was a small but significant increase in clinically relevant bleeding events, but fewer serious adverse events compared with LMWH regimens.

Another key difference between the two sets of guidelines is that the American Academy of Orthopaedic Surgeons places higher priority on wound complications, bleeding complications, and other adverse events that are exacerbated by chemotherapy, compared with the ACCP. These differences lead to different trials being included in the systematic reviews upon which the recommendations are made by the two associations.

The safety of initiating VTE prophylaxis with concurrent epidural analgesia must be considered in ERAS for joint arthroplasty. The incidence of clinically significant bleeding associated with neuraxial block and VTE thromboprophylaxis is unknown, but may be as high as 1:3000 in some populations. Neuraxial block is associated with neuraxial analgesia must be considered in ERAS for joint arthroplasty. The incidence of clinically significant bleeding associated with neuraxial block and VTE thromboprophylaxis is unknown, but may be as high as 1:3000 in some populations.

According to American Society of Regional Anesthesia and Pain Medicine guidelines, prophylactic LMWH should be given no less than 12 h before insertion or removal of an epidural catheter. American Society of Regional Anesthesia and Pain Medicine guidelines consistently recommend against twice daily LMWH dosing in the presence of an epidural catheter. The American Society of Regional Anesthesia and Pain Medicine additionally recommends withholding DOACs 3–5 days before performing a neuraxial block (depending on the drug), and waiting 6 h after oral administration (for all DOACs) for removal or manipulation of an epidural catheter.

Conclusions

Significant progress has been made in the application of ERAS to hip and knee arthroplasty. Decades of research have improved patient safety, improved outcomes, reduced length of hospital stay, and effected cost savings. However, there is still significant work to be done. Additional evidence is needed to confirm that adoption of ERAS protocols benefits hip and knee arthroplasty patients. Future research should focus on understanding which components contribute to improved recovery, and via what mechanism. Studies on individual components of ERAS and pathways implemented in totality need to be accompanied by audit of practices and processes. Given the significant improvements seen in other surgical subspecialties, further evaluation and adoption of ERAS pathways should be a priority for joint arthroplasty care teams.

Authors’ contributions

E.M.S. and J.T.Y. contributed equally to conceiving the idea, collecting data, and drafting and revising the manuscript.

Declaration of interest

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