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**Developing an enhanced recovery after surgery program for oncology patients who undergo hip or knee reconstruction surgery**

Bourazani M *et al*. ERAS pathways in orthopedic surgical oncology

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**Abstract**

Enhanced recovery after surgery (ERAS) protocols are applied in orthopedic surgery and are intended to reduce perioperative stress by implementing combined evidence-based practices with the cooperation of various health professionals as an interdisciplinary team. ERAS pathways include pre-operative patient counselling, regional anesthesia and analgesia techniques, post-operative pain management, early mobilization and early feeding. Studies have shown improvement in the recovery of patients who followed an ERAS program after hip or knee arthroplasty, compared with those who followed a traditional care approach. ERAS protocols reduce post-operative stress, contribute to rapid recovery, shorten length of stay (LOS) without increasing the complications or readmissions, improve patient satisfaction and decrease the hospital costs. We suggest that the ERAS pathway could reduce the LOS in hospital for patients undergoing total hip replacement or total knee replacement. These programs require good organization and handling by the multidisciplinary team. ERAS programs increase patient's satisfaction due to their active participation which they experience as personalized treatment. The aim of the study was to develop an ERAS protocol for oncology patients who undergo bone reconstruction surgeries using massive endoprosthesis, with a view to improving the surgical outcomes.

**Key Words:** Hip or knee replacement; Joint reconstruction; Enhanced recovery after orthopedic surgery; Fast-track orthopedic surgery; Enhanced recovery after surgery pathways in orthopedic surgery; Rehabilitation after hip or knee replacement

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**Core Tip:** Enhanced recovery after surgery (ERAS) pathways are applied to oncology patients undergoing primary total hip replacement or total knee replacement; and through evidenced practices are used by the multidisciplinary team, with the aim of reducing the perioperative stress and its effects. ERAS protocols have been reported to promote early recovery, early mobilization, early feeding, and better pain management with multimodal analgesia. ERAS pathways in orthopedic surgery, also, reduce postoperative length of stay, postoperative complications and mortality by 30 d after surgery, hospital costs, and readmission rate by 30 d after discharge.

**INTRODUCTION**

Orthopedic prosthesis has been used globally since the 1960s. The aim is to restore the function of the joint replaced and to improve the patient's quality of life[1]. The first primary hip arthroplasty with a metal prosthesis was performed in 1953 by the Englishman George McKee[2]. Since then, different interventions have been developed varying in terms of their design and construction material, for a number of joints, revolutionizing the specialty of orthopedics[3,4]. Nowadays, the use of orthopedic prostheses is very common. It is estimated that more than 600000 knee arthroplasties are performed in the United States each year[5].

Endoprostheses are used in two areas of orthopedics: (1) In reconstructions of joints, which have been damaged by trauma, degenerative or systemic diseases and need to be replaced by metal endoprosthesis (semi- arthroplasty of the hip, knee and shoulder, total ankle arthroplasty and total hip and knee arthroplasty) for better functional and long-term results[6]; and (2) In orthopedic oncology after tumor resection due to malignancies or, less often, benign diseases, where bone and tissue deficits are restored with extensive prosthesis. Until about 1970, the only treatment for bone tumors and soft tissue sarcomas was amputation, without improving patient survival though. Since then, rapid advances in prosthesis technological has allowed the rescue of limps, which in combination with chemotherapy have significantly improved the survival rate[7].

The idea of enhanced recovery pathways was first introduced by Kehlet in the late 1990s, improving the mental and physical effects of post-operative stress on the recovery and general clinical condition of a patient undergoing surgery[8,9]. The concept of fast-track surgery, as it is widely known, included a combination of minimally invasive surgical techniques, combined anesthesia and analgesia, early feeding and early mobilization[10,11]. It was initially applied to colorectal surgery and later to almost all general surgeries[12,13].

Nowadays, fast-track programs have evolved into enhanced recovery after surgery (ERAS) protocols applied by a variety of surgical specialties, including orthopedics. Studies have shown that ERAS protocols reduce length of stay (LOS) without increasing mortality, readmissions or complications rates, decrease hospital cost and enhance patient satisfaction[14,15].

ERAS protocols are intended to reduce perioperative stress, which causes metabolic and immune changes with side effects on the various body systems and increases susceptibility to post-operative infections[14,16,17]. This is achieved through a combination of multifactorial evidenced-based practices performed by various health specialties collaborating in an interdisciplinary team (surgeon, anesthesiologist, nurse, physiotherapist, *etc*.). An ERAS protocol is divided into three phases: Pre-operative, intraoperative, and post-operative (Table 1). It often begins before the patient’s admission to the hospital and continues after discharge. The active participation of patients is required throughout the program[17–19].

According to ERAS protocols, there are several components of perioperative care that affect stress response and accelerate recovery. These include pre-surgical counselling, short fasting period, early mobilization, bowel and bladder preparation, anesthesia and analgesia, thrombocytopenia, prevention of nausea and vomiting and fluid management[20].

**PRE-OPERATIVE PERIOD**

***Informed consent***

In order for the patient to follow an ERAS protocol, it is necessary to be informed about all the care practices they will receive, the expected results of their care and the active role they will play in the program, and be acquainted with all the members of the interdisciplinary team. Some patients feel reticent about new practices out of either ignorance or fear, so they disagree or need time to decide. The interdisciplinary team should answer each question of the patient and give them the written protocol instructions[16,20,21].

***Patient’s medical history and determination of vital signs***

After the diagnosis and before the surgery is decided by the surgeon, the multidisciplinary team meets the patient to determine their vital signs and identify any health conditions they may have that may be improved until the planned surgery[22,23]. Patients at high risk for post-operative complications are identified by calculating individual risk based on family history, symptoms, and health status measurement using specific questionnaires[24,25]. One such tool is the Revised Cardiac Risk Index (Lee Criteria), which assesses the risk of more serious heart events based on a history of ischemic heart disease, heart failure, stroke, insulin-dependent type II diabetes, serum creatinine > 177 μmol/L and high risk surgery[24,26–28]. There are many specialized tools for measuring a patient's physical function, severity of surgery and anesthesia, post-operative mortality and morbidity, as well as various measurements of frailty related to clinical outcomes from surgery, supported by the American Society of Anesthesiologists[26–28].

***Counseling***

ERAS protocols aim to increase the patient's physiological and functional reserves before surgery, which is, in fact, their main difference from fast-track protocols[11,29,30]. Studies have demonstrated the effectiveness of targeted pre- operative counseling. In particular, to reduce the risk of respiratory complications, such as infection or atelectasis, and the risk of post-operative wound inflammation, pre-operative smoking cessation within 2-4 wk of surgery is recommended[31,32]. If this is not possible, then it is recommended to reduce the number of cigarettes *per* day rather than quitting smoking, as this would result in a reflex increase in secretions that would have the opposite effect. Patients who consume alcohol have a slow recovery and increased rates of post-operative complications, so it is recommended to follow alcohol withdrawal programs before surgery when possible[33–35].

***Pre-operative fasting***

According to ERAS protocols, the routine of “being nil by mouth” from midnight before surgery to patients who are going to be operated is considered obsolete and incorrect. Fasting increases the peri-operative stress and its adverse effects as catabolism, insulin resistance and hyperglycemia[36,37]. ERAS protocols recommend shortening the pre-operative fasting time; clear fluid fasting for 2 h and solid food fasting for 6 h before surgery are enough for most patients. Patients with gastroparesis, esophageal achalasia or previous upper gastrointestinal surgery, morbid obesity and previous history of post-operative nausea and vomiting are excluded[38,39]. Pre-operative administration of oral carbohydrate drinks has been studied in recent years and shown to significantly improve insulin resistance without significant impact on the recovery time of patients undergoing hip or knee replacement surgery[40–42]. Although carbohydrate intake in orthopedic surgery has been shown to improve patients’ well-being, metabolism, and post-operative pain, it is not recommended as a standard practice[17,43,44].

***Pre-operative anemia management***

Pre-operative anemia should be evaluated and treated before surgery. Pre- operative anemia is associated with increased rates of allogeneic transfusion, longer stay in hospital, increased risk of post-operative infection, higher post- operative morbidity, complications and readmissions[45,46]. Clinical intervention studies about pre-operative and post-operative treatment with iron (Fe) or erythropoietin have reported statistically and clinically significant reduction in allogeneic blood transfusions[46–48]. The algorithm used to detect and correct pre- operative anemia by ERAS certified centers was associated with a reduction in the rate of transfusions, LOS, hospital readmissions, admissions to intensive care units and hospital cost[49].

**INTRA-OPERATIVE AND POST-OPERATIVE PERIODS**

***Anesthetic protocol***

In order to extract comparable results from an ERAS protocol, a standard anesthetic protocol must be followed. However, this is not always possible (for various reasons), which causes problems with regard to the homogeneity of parameters and the quality of the study methodology, thus challenging its reliability[50,51]. General anesthesia (GA) with total intravenous anesthesia using continuous drip infusion of Propofol and Remifentanil is recommended by ERAS pathways. In vitro studies have shown the properties of propofol as an anti-inflammatory agent and as a stimulant of immune response with beneficial effects on cancer recurrence prevention[52–55]. Oncology patients have peculiarities compared to the rest of the population. They are usually patients with metastatic or primary disease who have undergone chemotherapy and/or radiotherapy and have increased risk of intraoperative complications, especially during bone reconstruction with endoprosthesis and use of bone cement[56]. After a systematic review and meta-analysis of anesthesia techniques used for total knee replacement (TKR) and total hip replacement (THR) in non-cancer patients, the choice of anesthesia type was based on the type of surgery and the patient's general condition[57]. The level of evidence was low for GA or neuraxial anesthesia (NA), but the recommendation strength for both types of anesthesia was strong for patients undergoing hip or knee arthroplasty[52,58].

***Neuraxial Anesthesia***

The gold-standard of ERAS programs is the use of epidural or spinal anesthesia, but it is not recommended as a routine specifically for hip or knee replacement surgery[57,59,60]. There is a strong recommendation from the ERAS society not to inject high doses of opioids into epidural or spinal cord to avoid the risk of respiratory depression, post-operative nausea-vomiting (PONV), pruritus and urinary retention[61–63]. Morphine in low doses (0.1-0.18 mg) prevents the risk of respiratory depression and provides an adequate analgesic effect compared with continuous local anesthetic infusion after peripheral nerve blocks (PNB). NA with morphine promotes early patient mobilization[64]. Recent clinical trials using non- opioid formulations, such as bupivacaine, have shown excellent results with minimal risk of complications[51,65].

In ERAS protocols for hip or knee replacement, NA is recommended for its superiority over GA in reducing the stress response and the insulin resistance[19,66]. NA offers great analgesic benefits and reduces LOS and hospital costs, but may cause side effects such as respiratory depression, PONV and pruritus, therefore not recommended as a routine[19].

***Regional anesthesia/analgesia***

Regional anesthesia (RA) can reduce the incidence of cancer recurrence due to reduced need for opioids, suppression of the sympathetic nervous system, reduction of perioperative stress, and immediate anti-inflammatory and anticancer effect on immune system[54,67,68]. Although there are many studies that support the positive effects of RA on cancer recurrence, more studies are needed to determine the effects of RA on orthopedic cancers. Data may be incomplete, as orthopedic oncology procedures often involve resection of large bones and/or muscle groups and can take up to 12 h, making GA more common[69]. However, these resections can be performed using RA, either alone or in combination with GA[55,69].

RA provides a greater advantage in joint reconstruction as it delivers sufficient anesthesia for orthopedic surgery and great post-operative analgesia, inhibits the release of stress hormones and reduces insulin resistance. A multimodal approach to pain management with RA and multimodal analgesia (MA) is supported by ERAS protocols[17,68]. RA always plays an important role in minimizing the intra- operative requirements for opioids and should not be considered as an alternative to GA, but rather as a complement to an integrated strategy[68].

Morphine has a negative effect on the functioning of the immune system and it is strongly recommended to minimize doses[70–72]. MA is of paramount importance in the perioperative period, because it helps to reduce the need for opioids[73]. Opioid sparing analgesia based on intravenous lidocaine, nonsteroidal anti-inflammatory drugs (NSAIDs) and ketamine has been found to maintain immune function[73].

RA seems to benefit most elderly and debilitated or seriously ill patients or those undergoing major orthopedic and thoracic surgeries[74]. Recent studies have shown that total arthroplasty may be possible with the use of RA in all age groups, regardless of the severity of the comorbidity[58,67].

ERAS programs significantly reduced the incidence of post-operative complications, such as myocardial ischemia and mortality, over a period of 30 d compared to conventional treatment[58,66].

***Intra-operative analgesia***

For purpose of pain management, using a combination of NSAIDs or inhibitors of cyclooxygenase-2 (COX-2) with paracetamol (acetaminophen) is recommended to significantly reduce the administration of opioid drugs in the context of a MA[21,75,76]. Concomitant use of paracetamol and NSAIDs is the main axis of perioperative MA and one of the most important components of ERAS[73,76]. Studies have shown that MA has great analgesic effects on moderate pain and reduces the additional use of opioids after TKR and THR[57,77]. NSAIDs and COX-2 inhibitors are not recommended for patients with contraindications (allergy, pre-existing kidney disease, *etc.*)[78].

***Optimal intra-operative fluid management***

Intravenous fluids and maintenance of normovolemia are very important for perioperative patients. Failure to maintain normovolemia may lead to increased morbidity/mortality, affect tissue oxygenation, increase post-operative cardiopulmonary complications, increase trauma inflammation and prolong hospital stay[17,19,21]. Intra-operative isotonic crystalline fluids are administered to preserve homeostasis and the electrolyte balance at a rate of 3-5 mL/kg/h. ERAS society recommends early transition from IV to PO fluid therapy within 24 h for patients undergoing major surgery[79].

***Prevention and treatment of PONV***

PONV is undoubtedly an unpleasant adverse effect, which is experienced by 20%-30% of surgical patients and 70% of high-risk patients (patients with gastroparesis, esophageal achalasia, dysphagia, neurological diseases, gastrointestinal surgery, Whipple procedure, gastrectomy, *etc.*)[38]. For the prevention and treatment of PONV, it is recommended to administer 4 mg IV infusion of ondansetron before induction of anesthesia and metoclopramide half an hour before awakening. Especially for high-risk patients, a combination of 2-3 antiemetics is recommended. Such a combination may be ondansetron 4mg overnight, dexamethasone 4-5 mg after induction of anesthesia and droperidol 0.625-1.25 mg at the end of surgery[17,19,21,80]. Caution is needed in the use of dexamethasone as an antiemetic in oncology patients because of its potential immunosuppressive and hyperglycemic effects[81]. A recent study has shown that dexamethasone significantly decreased the incidences of PONV as well as pain, improved respiratory parameters, and reduced the need for additional post-operative analgesic and antiemetic drugs[81]. It is worth noting that Gan *et al*[80] andSherif *et al*[82] created a simplified PONV probability scoring system using only four risk factors: (1) Female gender; (2) Previous PONV history; (3) Smoking; and (4) Opioid analgesics[80,82]. Therefore, a combination of two drugs is recommended for patients with one or two risk factors, while for patients with more than two factors the recommendation is a combination of three drugs[80,83]. Finally, chewing gum post- operatively appears to help mobilize the gastrointestinal system[84].

***Normothermia***

Hypothermia affects over 60% of patients. Maintaining body temperature at normal levels throughout the surgery has been shown to help reduce post- operative wound infection, intraoperative bleeding, cardiovascular complications, post-operative stress and its metabolic effects[85,86]. Prevention of perioperative hypothermia is achieved by using electric hot air devices for the patient's body and fluid heating pumps to administer intravenous fluids or blood products at 37-40 ℃ intraoperatively. The temperature in the operating room should be 21 ℃ for total joint surgeries[19,86–89].

***Prophylactic anticoagulant treatment***

There is a significant correlation between deep vein thrombosis, pulmonary embolism and hip and knee replacement surgery, which can lead to post- thrombotic syndrome or even death[90]. The NICE guidelines recommend early mobilization and fast return to baseline activity[61], as well as low-molecular-weight heparin anticoagulant therapy for 28 d in hip surgeries and 14 d in total knee operations[90–92].

***Antimicrobial prophylaxis***

One of the most serious and harmful post-operative complications in orthopedic surgery is bone tissue and prosthetic joint infections. Infection after THR or TKR surgery is called osteomyelitis and remains to date the worst complication to treat[21,93]. Bone infection treatment often requires removal of the prosthesis in order to reduce osteolysis and inflammation[94–97]. Recommendation for prophylactic antimicrobial therapy is 1st or 2nd generation cephalosporin (Cefazolin, Cefuroxime) 30-60 min before the skin incision as a single-dose, depending on the patient's weight (weight-adjusted dose)[98].

***Surgical management***

Although there are many comparative studies on surgical techniques and approaches to TKR and THR, we cannot conclude with certainty which technique is superior to all. ERAS society does not recommend a specific surgical technique[16].

ERAS protocols recommend avoiding the use of tourniquets and drains as a routine. It seems that tourniquet does not reduce the total blood loss from surgery, while increasing the risk of thromboembolic events, edema and complications[99–101]. Regarding wound drainage, studies show that not only does it not help prevent hematomas, but it also increases the risk of inflammation and blood loss because it eliminates the tamponade effect and may cause a retrograde infection[102–104].

***Post-operative analgesia***

Effective post-operative pain management includes a combination of analgesic drugs with central and peripheral action, aimed at early mobilization and feeding. Once the patient begins to eat solid food, the IV analgesic regimen should be administered *per* os[19,36]. In ERAS protocols, MA is very important for pain management, enhanced recovery and patients discharge. MA significantly reduces the opioid requirements and helps reduce PONV, post-operative stress and the risk of complications[16,19]. The use of paracetamol in combination with lornoxicam or celecoxib/parecoxib is recommended. Paracetamol is very effective in acute post-operative pain without significant side effects and constitutes a key component of MA in all ERAS guidelines[17,78,105].

***Prevention of in-hospital falls after surgery***

RA is responsible for in-hospital falls in post-operative patient after TKR and THR. Patients with GA have a higher rate of in-hospital falls compared to NA. The group of PNB has not been significantly associated with patients’ falls[67], while PNB-induced quadriceps insufficiency is not the only cause for in-hospital falls[106]. Many factors can contribute to an in-hospital fall after TKR and THR, such as re-operation, advanced age, female gender and comorbidities, which highlights the importance of establishing a multidisciplinary in-hospital fall prevention program in every orthopedic ward[35,107,108].

Multimodal post-operative analgesia, including RA or PNB techniques, in combination with goal-directed rehabilitation are important components that prevent in-hospital falls. This approach accelerates functional recovery and minimizes the risk of in-hospital falls, increases patient satisfaction and reduces overall hospital stay and costs[109,110].

**PHYSIOTHERAPY REHABILITATION**

Physiotherapy rehabilitation of patients after TKR or THR surgery should begin much earlier than the day of surgery, in the form of counseling. After the physical evaluation, interventions are made to reduce body mass index and increase muscle strength by increasing physical exercise and activity[71,111]. The procedure can be started up to 4 wk before scheduled surgery, with regular sessions aimed at early mobilization. Patients are initially informed in detail about the surgery and the post-operative stage even with appropriate leaflets. If possible, patient counseling can be performed simultaneously to a group of people who will undergo surgery on the same day. At the same time, an exercise and stretching program can be implemented to strengthen the muscles of the lower extremities of patients, who learn how to perform it on their own[112,113].

Patients who have followed a counseling program delivered by the physiotherapist, have become more comfortable with the use of walking-aid, made the suggested interventions in the configuration of their residence so that it is safe for a faster return home and have returned home on the 3rd post-operative day without complications[114,115].

The strengthening part is very important because patients who are going to undergo TKR or THR surgery, already have deficient function of the quadriceps due to arthritis or cancer. This is caused by reduced functional use of the joint due to pain and atrophy. Muscle strengthening with progressively increasing resistance and neuromuscular electrical stimulation perioperatively have been shown to improve the functional performance of the quadriceps[116].

Pre-operative mobilization and strengthening seems to be crucial because there is a significant reduction in muscle strength and ability to perform the leg press test within the 1st week after surgery[117]. In fact, the decrease is not due to objective findings (inflammation, swelling) but subjective symptoms (insecurity, pain), which subside to such an extent when applying the pre-operative approach and early mobilization, that patients are discharged earlier and, in some cases, do not need post-operative physiotherapy other than an exercise routine they are trained to perform at home[118,119].

Psychological support of the patients from the interdisciplinary team is necessary, because it increases their sense of security and satisfaction[120]. The team reports on the benefits of early mobilization within 8-12 h after the surgery. Even patients who disagree or hesitate to follow the instructions of physiotherapists should at least agree to cooperate. Their initial reluctance is followed by surprise, as they experience less pain than they thought during the recovery period and are satisfied with their post-operative progress[121].

Early mobilization reduces the LOS as patients can be discharged sooner without increasing the risk of complications. Depending on the pain experienced by the patient, he or she may be able to stand or walk without aid on post- operative day 1 if the visual analogue scale score is lower than 5[122].

Pain management, reduced swelling, autonomous movement and normal mobilization with walking-aids are criteria for the patient's discharge from the hospital. Indicatively, following TKR the aim is for the patient to be able to lift their limb with stretched knee and achieve pain-free flexion to 90 degrees, while safe and controlled walking to and from the bed suffices after THR surgery[111,115,122]. Post-operatively, standard physiotherapy (kinesiotherapy) as well as other methods, including electrical stimulation, are applied in order to strengthen the muscles, increase the range of motion, reduce swelling and enhance independent gait[123,124].

All of the above ERAS pathways that developed for the rapid postoperative recovery of oncological patients undergoing Total Knee or Hip Reconstruction are summarized in Table 1.

**CONCLUSION**

ERAS programs undoubtedly reduce hospitalization days without increasing the risk of complications or relapses and reduces hospital costs. These programs require good organization and handling by the multidisciplinary team. Nurses have a central role in the implementation of ERAS programs. ERAS programs increase the patient's sense of satisfaction due to their active participation which they experience as an individualized treatment. However, their implementation is not common practice in Greece, so additional multicenter clinical trials at are required.

**REFERENCES**

1 **Laupacis A**, Bourne R, Rorabeck C, Feeny D, Wong C, Tugwell P, Leslie K, Bullas R. The effect of elective total hip replacement on health-related quality of life. *J Bone Joint Surg Am* 1993; **75**: 1619-1626 [PMID: 8245054 DOI: 10.2106/00004623-199311000-00006]

2 **Knight SR**, Aujla R, Biswas SP. Total Hip Arthroplasty - over 100 years of operative history. *Orthop Rev (Pavia)* 2011; **3**: e16 [PMID: 22355482 DOI: 10.4081/or.2011.e16]

3 **Learmonth ID**, Young C, Rorabeck C. The operation of the century: total hip replacement. *Lancet* 2007; **370**: 1508-1519 [PMID: 17964352 DOI: 10.1016/S0140-6736(07)60457-7]

4 **Wang W**, Ouyang Y, Poh CK. Orthopaedic implant technology: biomaterials from past to future. *Ann Acad Med Singap* 2011; **40**: 237-244 [PMID: 21678015]

5 **Brophy RH**, Gray BL, Nunley RM, Barrack RL, Clohisy JC. Total knee arthroplasty after previous knee surgery: expected interval and the effect on patient age. *J Bone Joint Surg Am* 2014; **96**: 801-805 [PMID: 24875020 DOI: 10.2106/JBJS.M.00105]

6 **Karachalios T**, Komnos G, Koutalos A. Total hip arthroplasty: Survival and modes of failure. *EFORT Open Rev* 2018; **3**: 232-239 [PMID: 29951261 DOI: 10.1302/2058-5241.3.170068]

7 **Hwang JS**, Mehta AD, Yoon RS, Beebe KS. From amputation to limb salvage reconstruction: evolution and role of the endoprosthesis in musculoskeletal oncology. *J Orthop Traumatol* 2014; **15**: 81-86 [PMID: 24057576 DOI: 10.1007/s10195-013-0265-8]

8 **Kehlet H**, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. *Ann Surg* 2008; **248**: 189-198 [PMID: 18650627 DOI: 10.1097/SLA.0b013e31817f2c1a]

9 **Kehlet H**, Thienpont E. Fast-track knee arthroplasty -- status and future challenges. *Knee* 2013; **20 Suppl 1**: S29-S33 [PMID: 24034592 DOI: 10.1016/S0968-0160(13)70006-1]

10 **Buvanendran A**, Kroin JS. Multimodal analgesia for controlling acute postoperative pain. *Curr Opin Anaesthesiol* 2009; **22**: 588-593 [PMID: 19606021 DOI: 10.1097/ACO.0b013e328330373a]

11 **Bourazani M,** Karopoulou E, Fyrfiris N, Poulopoulou S, Papatheodorou D. EP1096 Implementing enhanced recovery after surgery (ERAS) pathways in major gynecologic oncology operations in Greece (The pre-eliminary results of our department). *Int J Gynecol Cancer* 2019; **29:** 573-574 [DOI: 10.1136/ijgc-2019-ESGO.1138]

12 **Moningi S**, Patki A, Padhy N, Ramachandran G. Enhanced recovery after surgery: An anesthesiologist's perspective. *J Anaesthesiol Clin Pharmacol* 2019; **35**: S5-S13 [PMID: 31142953 DOI: 10.4103/joacp.JOACP\_238\_16]

13 **Visioni A,** Shah R, Gabriel E, Attwood K, Kukar M, Nurkin S. Enhanced Recovery After Surgery for Noncolorectal Surgery?: A Systematic Review and Meta-analysis of Major Abdominal Surgery. *Ann Surg* 2018; **267**: 57-65 [PMID: 28437313 DOI: 10.1097/SLA.0000000000002267]

14 **Auyong DB**, Allen CJ, Pahang JA, Clabeaux JJ, MacDonald KM, Hanson NA. Reduced Length of Hospitalization in Primary Total Knee Arthroplasty Patients Using an Updated Enhanced Recovery After Orthopedic Surgery (ERAS) Pathway. *J Arthroplasty* 2015; **30**: 1705-1709 [PMID: 26024988 DOI: 10.1016/j.arth.2015.05.007]

15 **Stambough JB**, Nunley RM, Curry MC, Steger-May K, Clohisy JC. Rapid recovery protocols for primary total hip arthroplasty can safely reduce length of stay without increasing readmissions. *J Arthroplasty* 2015; **30**: 521-526 [PMID: 25683296 DOI: 10.1016/j.arth.2015.01.023]

16 **Zhu S**, Qian W, Jiang C, Ye C, Chen X. Enhanced recovery after surgery for hip and knee arthroplasty: a systematic review and meta-analysis. *Postgrad Med J* 2017; **93**: 736-742 [PMID: 28751437 DOI: 10.1136/postgradmedj-2017-134991]

17 **Kaye AD,** Urman RD, Cornett EM, Hart BM, Chami A, Gayle JA, Fox CJ. Enhanced recovery pathways in orthopedic surgery. *J Anaesthesiol Clin Pharmacol* 2019; **35:** S35-S39 [PMID: 31142957 DOI: 10.4103/joacp.JOACP\_35\_18]

18 **Gibb ACN**, Crosby MA, McDiarmid C, Urban D, Lam JYK, Wales PW, Brockel M, Raval M, Offringa M, Skarsgard ED, Wester T, Wong K, de Beer D, Nelson G, Brindle ME. Creation of an Enhanced Recovery After Surgery (ERAS) Guideline for neonatal intestinal surgery patients: a knowledge synthesis and consensus generation approach and protocol study. *BMJ Open* 2018; **8**: e023651 [PMID: 30530586 DOI: 10.1136/bmjopen-2018-023651]

19 **Wainwright TW**, Gill M, McDonald DA, Middleton RG, Reed M, Sahota O, Yates P, Ljungqvist O. Consensus statement for perioperative care in total hip replacement and total knee replacement surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Acta Orthop* 2020; **91**: 3-19 [PMID: 31663402 DOI: 10.1080/17453674.2019.1683790]

20 **Tan NLT**, Hunt JL, Gwini SM. Does implementation of an enhanced recovery after surgery program for hip replacement improve quality of recovery in an Australian private hospital: a quality improvement study. *BMC Anesthesiol* 2018; **18**: 64 [PMID: 29898653 DOI: 10.1186/s12871-018-0525-5]

21 **Ghosh A**, Chatterji U. An evidence-based review of enhanced recovery after surgery in total knee replacement surgery. *J Perioper Pract* 2019; **29**: 281-290 [PMID: 30212288 DOI: 10.1177/1750458918791121]

22 **McLeod RS**, Aarts MA, Chung F, Eskicioglu C, Forbes SS, Conn LG, McCluskey S, McKenzie M, Morningstar B, Nadler A, Okrainec A, Pearsall EA, Sawyer J, Siddique N, Wood T. Development of an Enhanced Recovery After Surgery Guideline and Implementation Strategy Based on the Knowledge-to-action Cycle. *Ann Surg* 2015; **262**: 1016-1025 [PMID: 25692358 DOI: 10.1097/SLA.0000000000001067]

23 **Committee on Standards and Practice Parameters**, Apfelbaum JL, Connis RT, Nickinovich DG; American Society of Anesthesiologists Task Force on Preanesthesia Evaluation, Pasternak LR, Arens JF, Caplan RA, Connis RT, Fleisher LA, Flowerdew R, Gold BS, Mayhew JF, Nickinovich DG, Rice LJ, Roizen MF, Twersky RS. Practice advisory for preanesthesia evaluation: an updated report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. *Anesthesiology* 2012; **116**: 522-538 [PMID: 22273990 DOI: 10.1097/ALN.0b013e31823c1067]

24 **Boersma E**, Kertai MD, Schouten O, Bax JJ, Noordzij P, Steyerberg EW, Schinkel AF, van Santen M, Simoons ML, Thomson IR, Klein J, van Urk H, Poldermans D. Perioperative cardiovascular mortality in noncardiac surgery: validation of the Lee cardiac risk index. *Am J Med* 2005; **118**: 1134-1141 [PMID: 16194645 DOI: 10.1016/j.amjmed.2005.01.064]

25 **Jørgensen CC**, Kehlet H; Lundbeck Foundation Centre for Fast-track Hip and Knee Replacement Collaborative Group. Role of patient characteristics for fast-track hip and knee arthroplasty. *Br J Anaesth* 2013; **110**: 972-980 [PMID: 23365109 DOI: 10.1093/bja/aes505]

26 **Glance LG**, Lustik SJ, Hannan EL, Osler TM, Mukamel DB, Qian F, Dick AW. The Surgical Mortality Probability Model: derivation and validation of a simple risk prediction rule for noncardiac surgery. *Ann Surg* 2012; **255**: 696-702 [PMID: 22418007 DOI: 10.1097/SLA.0b013e31824b45af]

27 **Doyle DJ,** Goyal A, Bansal P, Garmon EH. American Society of Anesthesiologists Classification. 2020 Jul 4. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan [PMID: 28722969]

28 **Fitz-Henry J**. The ASA classification and peri-operative risk. *Ann R Coll Surg Engl* 2011; **93**: 185-187 [PMID: 21477427 DOI: 10.1308/rcsann.2011.93.3.185a]

29 **Hoorntje A**, Koenraadt KLM, Boevé MG, van Geenen RCI. Outpatient unicompartmental knee arthroplasty: who is afraid of outpatient surgery? *Knee Surg Sports Traumatol Arthrosc* 2017; **25**: 759-766 [PMID: 28229182 DOI: 10.1007/s00167-017-4440-y]

30 **Ibrahim MS**, Twaij H, Giebaly DE, Nizam I, Haddad FS. Enhanced recovery in total hip replacement: a clinical review. *Bone Joint J* 2013; **95-B**: 1587-1594 [PMID: 24293586 DOI: 10.1302/0301-620X.95B12.31303]

31 **Akhavan S**, Nguyen LC, Chan V, Saleh J, Bozic KJ. Impact of Smoking Cessation Counseling Prior to Total Joint Arthroplasty. *Orthopedics* 2017; **40**: e323-e328 [PMID: 28027387 DOI: 10.3928/01477447-20161219-02]

32 **Mak JC**, Fransen M, Jennings M, March L, Mittal R, Harris IA; National Health and Medical Research Council (NHMRC) of Australia. Evidence-based review for patients undergoing elective hip and knee replacement. *ANZ J Surg* 2014; **84**: 17-24 [PMID: 23496209 DOI: 10.1111/ans.12109]

33 **Best MJ**, Buller LT, Gosthe RG, Klika AK, Barsoum WK. Alcohol Misuse is an Independent Risk Factor for Poorer Postoperative Outcomes Following Primary Total Hip and Total Knee Arthroplasty. *J Arthroplasty* 2015; **30**: 1293-1298 [PMID: 25769745 DOI: 10.1016/j.arth.2015.02.028]

34 **Oppedal K**, Møller AM, Pedersen B, Tønnesen H. Preoperative alcohol cessation prior to elective surgery. *Cochrane Database Syst Rev* 2012: CD008343 [PMID: 22786514 DOI: 10.1002/14651858.CD008343.pub2]

35 **Jørgensen CC**, Petersen MA, Kehlet H; Lundbeck Foundation Centre for Fast-Track Hip and Knee Replacement Collaborative Group. Preoperative prediction of potentially preventable morbidity after fast-track hip and knee arthroplasty: a detailed descriptive cohort study. *BMJ Open* 2016; **6**: e009813 [PMID: 26758264 DOI: 10.1136/bmjopen-2015-009813]

36 **Weimann A**, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, Laviano A, Ljungqvist O, Lobo DN, Martindale R, Waitzberg DL, Bischoff SC, Singer P. ESPEN guideline: Clinical nutrition in surgery. *Clin Nutr* 2017; **36**: 623-650 [PMID: 28385477 DOI: 10.1016/j.clnu.2017.02.013]

37 **Schricker T**, Lattermann R. Perioperative catabolism. *Can J Anaesth* 2015; **62**: 182-193 [PMID: 25588775 DOI: 10.1007/s12630-014-0274-y]

38 **Bourazani M,** Kelesi M, Fasoi G. Enhanced Recovery after Surgery (ERAS) protocols in breast cancer patients undergoing post-mastectomy breast reconstruction with tissue expander. *Hell J Nurs Sci* 2019; **12:** 14-22 [DOI: 10.24283/hjns.20192.8-9]

39 **Smith I**, Kranke P, Murat I, Smith A, O'Sullivan G, Søreide E, Spies C, in't Veld B; European Society of Anaesthesiology. Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2011; **28**: 556-569 [PMID: 21712716 DOI: 10.1097/EJA.0b013e3283495ba1]

40 **Amer MA**, Smith MD, Herbison GP, Plank LD, McCall JL. Network meta-analysis of the effect of preoperative carbohydrate loading on recovery after elective surgery. *Br J Surg* 2017; **104**: 187-197 [PMID: 28000931 DOI: 10.1002/bjs.10408]

41 **Smith MD**, McCall J, Plank L, Herbison GP, Soop M, Nygren J. Preoperative carbohydrate treatment for enhancing recovery after elective surgery. *Cochrane Database Syst Rev* 2014: CD009161 [PMID: 25121931 DOI: 10.1002/14651858.CD009161.pub2]

42 **Harsten A**, Hjartarson H, Toksvig-Larsen S. Total hip arthroplasty and perioperative oral carbohydrate treatment: a randomised, double-blind, controlled trial. *Eur J Anaesthesiol* 2012; **29**: 271-274 [PMID: 22450530 DOI: 10.1097/EJA.0b013e3283525ba9]

43 **Harsten A.** Perioperative regimes for patients undergoing elective hip or knee arthroplasties. *Acta Anaesthesiol Scand* 2014; **58:** 12325 [DOI: 10.1111/aas.12325]

44 **Greenshields N,** Mythen M. Enhanced Recovery After Surgery. *Curr Anesthesiol Rep* 2020; **10:** 49-55 [DOI: 10.1007/s40140-020-00372-y]

45 **Kehlet H**. Fast-track hip and knee arthroplasty. *Lancet* 2013; **381**: 1600-1602 [PMID: 23663938 DOI: 10.1016/S0140-6736(13)61003-X]

46 **Muñoz M**, Gómez-Ramírez S, Cuenca J, García-Erce JA, Iglesias-Aparicio D, Haman-Alcober S, Ariza D, Naveira E. Very-short-term perioperative intravenous iron administration and postoperative outcome in major orthopedic surgery: a pooled analysis of observational data from 2547 patients. *Transfusion* 2014; **54**: 289-299 [PMID: 23581484 DOI: 10.1111/trf.12195]

47 **Gómez-Ramírez S**, Maldonado-Ruiz MÁ, Campos-Garrigues A, Herrera A, Muñoz M. Short-term perioperative iron in major orthopedic surgery: state of the art. *Vox Sang* 2019; **114**: 3-16 [PMID: 30411362 DOI: 10.1111/vox.12718]

48 **Theusinger OM**, Kind SL, Seifert B, Borgeat L, Gerber C, Spahn DR. Patient blood management in orthopaedic surgery: a four-year follow-up of transfusion requirements and blood loss from 2008 to 2011 at the Balgrist University Hospital in Zurich, Switzerland. *Blood Transfus* 2014; **12**: 195-203 [PMID: 24931841 DOI: 10.2450/2014.0306-13]

49 **Pujol-Nicolas A**, Morrison R, Casson C, Khan S, Marriott A, Tiplady C, Kotze A, Gray W, Reed M. Preoperative screening and intervention for mild anemia with low iron stores in elective hip and knee arthroplasty. *Transfusion* 2017; **57**: 3049-3057 [PMID: 29106698 DOI: 10.1111/trf.14372]

50 **Buggy DJ**, Freeman J, Johnson MZ, Leslie K, Riedel B, Sessler DI, Kurz A, Gottumukkala V, Short T, Pace N, Myles PS; StEP-COMPAC Group. Systematic review and consensus definitions for standardised endpoints in perioperative medicine: postoperative cancer outcomes. *Br J Anaesth* 2018; **121**: 38-44 [PMID: 29935592 DOI: 10.1016/j.bja.2018.03.020]

51 **Kehlet H**, Aasvang EK. Regional or general anesthesia for fast-track hip and knee replacement - what is the evidence? *F1000Res* 2015; **4** [PMID: 26918127 DOI: 10.12688/f1000research.7100.1]

52 **Wall T**, Sherwin A, Ma D, Buggy DJ. Influence of perioperative anaesthetic and analgesic interventions on oncological outcomes: a narrative review. *Br J Anaesth* 2019; **123**: 135-150 [PMID: 31255291 DOI: 10.1016/j.bja.2019.04.062]

53 **Fodale V**, D'Arrigo MG, Triolo S, Mondello S, La Torre D. Anesthetic techniques and cancer recurrence after surgery. *ScientificWorldJournal* 2014; **2014**: 328513 [PMID: 24683330 DOI: 10.1155/2014/328513]

54 **Cassinello F**, Prieto I, del Olmo M, Rivas S, Strichartz GR. Cancer surgery: how may anesthesia influence outcome? *J Clin Anesth* 2015; **27**: 262-272 [PMID: 25769963 DOI: 10.1016/j.jclinane.2015.02.007]

55 **Kim R**. Anesthetic technique and cancer recurrence in oncologic surgery: unraveling the puzzle. *Cancer Metastasis Rev* 2017; **36**: 159-177 [PMID: 27866303 DOI: 10.1007/s10555-016-9647-8]

56 **Anderson MR**, Jeng CL, Wittig JC, Rosenblatt MA. Anesthesia for patients undergoing orthopedic oncologic surgeries. *J Clin Anesth* 2010; **22**: 565-572 [PMID: 21056818 DOI: 10.1016/j.jclinane.2010.02.011]

57 **Moucha CS**, Weiser MC, Levin EJ. Current Strategies in Anesthesia and Analgesia for Total Knee Arthroplasty. *J Am Acad Orthop Surg* 2016; **24**: 60-73 [PMID: 26803543 DOI: 10.5435/JAAOS-D-14-00259]

58 **Memtsoudis SG**, Cozowicz C, Bekeris J, Bekere D, Liu J, Soffin EM, Mariano ER, Johnson RL, Hargett MJ, Lee BH, Wendel P, Brouillette M, Go G, Kim SJ, Baaklini L, Wetmore D, Hong G, Goto R, Jivanelli B, Argyra E, Barrington MJ, Borgeat A, De Andres J, Elkassabany NM, Gautier PE, Gerner P, Gonzalez Della Valle A, Goytizolo E, Kessler P, Kopp SL, Lavand'Homme P, MacLean CH, Mantilla CB, MacIsaac D, McLawhorn A, Neal JM, Parks M, Parvizi J, Pichler L, Poeran J, Poultsides LA, Sites BD, Stundner O, Sun EC, Viscusi ER, Votta-Velis EG, Wu CL, Ya Deau JT, Sharrock NE. Anaesthetic care of patients undergoing primary hip and knee arthroplasty: consensus recommendations from the International Consensus on Anaesthesia-Related Outcomes after Surgery group (ICAROS) based on a systematic review and meta-analysis. *Br J Anaesth* 2019; **123**: 269-287 [PMID: 31351590 DOI: 10.1016/j.bja.2019.05.042]

59 **Memtsoudis SG**, Rasul R, Suzuki S, Poeran J, Danninger T, Wu C, Mazumdar M, Vougioukas V. Does the impact of the type of anesthesia on outcomes differ by patient age and comorbidity burden? *Reg Anesth Pain Med* 2014; **39**: 112-119 [PMID: 24509423 DOI: 10.1097/AAP.0000000000000055]

60 **Rawal N**. Epidural technique for postoperative pain: gold standard no more? *Reg Anesth Pain Med* 2012; **37**: 310-317 [PMID: 22531384 DOI: 10.1097/AAP.0b013e31825735c6]

61 **Fernandez MA**, Karthikeyan S, Wyse M, Foguet P. The incidence of postoperative urinary retention in patients undergoing elective hip and knee arthroplasty. *Ann R Coll Surg Engl* 2014; **96**: 462-465 [PMID: 25198980 DOI: 10.1308/003588414X13946184902523]

62 **Theodoraki K,** Moka E, Argyra E, Siafaka I, Vadalouca A. Pro con debate 2: Regional anaesthesia has significantly improved outcome after major orthopedic, abdominal and thoracic surgery. *Reg Anesth Pain Med* 2017; **42:** 1

63 **Gehling M**, Tryba M. Risks and side-effects of intrathecal morphine combined with spinal anaesthesia: a meta-analysis. *Anaesthesia* 2009; **64**: 643-651 [PMID: 19462494 DOI: 10.1111/j.1365-2044.2008.05817.x]

64 **Tang Y**, Tang X, Wei Q, Zhang H. Intrathecal morphine versus femoral nerve block for pain control after total knee arthroplasty: a meta-analysis. *J Orthop Surg Res* 2017; **12**: 125 [PMID: 28814320 DOI: 10.1186/s13018-017-0621-0]

65 **Andersen LØ**, Kehlet H. Analgesic efficacy of local infiltration analgesia in hip and knee arthroplasty: a systematic review. *Br J Anaesth* 2014; **113**: 360-374 [PMID: 24939863 DOI: 10.1093/bja/aeu155]

66 **Khan SK**, Malviya A, Muller SD, Carluke I, Partington PF, Emmerson KP, Reed MR. Reduced short-term complications and mortality following Enhanced Recovery primary hip and knee arthroplasty: results from 6,000 consecutive procedures. *Acta Orthop* 2014; **85**: 26-31 [PMID: 24359028 DOI: 10.3109/17453674.2013.874925]

67 **Elkassabany NM**, Memtsoudis SG, Mariano ER. What Can Regional Anesthesiology and Acute Pain Medicine Learn from "Big Data"? *Anesthesiol Clin* 2018; **36**: 467-478 [PMID: 30092941 DOI: 10.1016/j.anclin.2018.04.003]

68 **Albrecht E**, Chin KJ. Advances in regional anaesthesia and acute pain management: a narrative review. *Anaesthesia* 2020; **75 Suppl 1**: e101-e110 [PMID: 31903582 DOI: 10.1111/anae.14868]

69 **Sen S**, Koyyalamudi V, Smith DD, Weis RA, Molloy M, Spence AL, Kaye AJ, Labrie-Brown CC, Morgan Hall O, Cornett EM, Kaye AD. The role of regional anesthesia in the propagation of cancer: A comprehensive review. *Best Pract Res Clin Anaesthesiol* 2019; **33**: 507-522 [PMID: 31791567 DOI: 10.1016/j.bpa.2019.07.004]

70 **Moyano J**, Aguirre L. Opioids in the immune system: from experimental studies to clinical practice. *Rev Assoc Med Bras (1992)* 2019; **65**: 262-269 [PMID: 30892453 DOI: 10.1590/1806-9282.65.2.262]

71 **Ondrovics M**, Hoelbl-Kovacic A, Fux DA. Opioids: Modulators of angiogenesis in wound healing and cancer. *Oncotarget* 2017; **8**: 25783-25796 [PMID: 28445930 DOI: 10.18632/oncotarget.15419]

72 **Plein LM**, Rittner HL. Opioids and the immune system - friend or foe. *Br J Pharmacol* 2018; **175**: 2717-2725 [PMID: 28213891 DOI: 10.1111/bph.13750]

73 **Missair A**, Cata JP, Votta-Velis G, Johnson M, Borgeat A, Tiouririne M, Gottumukkala V, Buggy D, Vallejo R, Marrero EB, Sessler D, Huntoon MA, Andres J, Casasola OL. Impact of perioperative pain management on cancer recurrence: an ASRA/ESRA special article. *Reg Anesth Pain Med* 2019; **44**: 13-28 [PMID: 30640648 DOI: 10.1136/rapm-2018-000001]

74 **Neuman MD**, Silber JH, Elkassabany NM, Ludwig JM, Fleisher LA. Comparative effectiveness of regional versus general anesthesia for hip fracture surgery in adults. *Anesthesiology* 2012; **117**: 72-92 [PMID: 22713634 DOI: 10.1097/ALN.0b013e3182545e7c]

75 **Mammoto T**, Fujie K, Mamizuka N, Taguchi N, Hirano A, Yamazaki M, Ueno S, Ma E, Hashimoto K. Effects of postoperative administration of celecoxib on pain management in patients after total knee arthroplasty: study protocol for an open-label randomized controlled trial. *Trials* 2016; **17**: 45 [PMID: 26803746 DOI: 10.1186/s13063-015-1106-2]

76 **Gelman D**, Gelmanas A, Urbanaitė D, Tamošiūnas R, Sadauskas S, Bilskienė D, Naudžiūnas A, Širvinskas E, Benetis R, Macas A. Role of Multimodal Analgesia in the Evolving Enhanced Recovery after Surgery Pathways. *Medicina (Kaunas)* 2018; **54** [PMID: 30344251 DOI: 10.3390/medicina54020020]

77 **Bian YY**, Wang LC, Qian WW, Lin J, Jin J, Peng HM, Weng XS. Role of Parecoxib Sodium in the Multimodal Analgesia after Total Knee Arthroplasty: A Randomized Double-blinded Controlled Trial. *Orthop Surg* 2018; **10**: 321-327 [PMID: 30485685 DOI: 10.1111/os.12410]

78 **Soffin EM**, YaDeau JT. Enhanced recovery after surgery for primary hip and knee arthroplasty: a review of the evidence. *Br J Anaesth* 2016; **117**: iii62-iii72 [PMID: 27940457 DOI: 10.1093/bja/aew362]

79 **Miller TE**, Myles PS. Perioperative Fluid Therapy for Major Surgery. *Anesthesiology* 2019; **130**: 825-832 [PMID: 30789364 DOI: 10.1097/ALN.0000000000002603]

80 **Gan TJ**, Diemunsch P, Habib AS, Kovac A, Kranke P, Meyer TA, Watcha M, Chung F, Angus S, Apfel CC, Bergese SD, Candiotti KA, Chan MT, Davis PJ, Hooper VD, Lagoo-Deenadayalan S, Myles P, Nezat G, Philip BK, Tramèr MR; Society for Ambulatory Anesthesia. Consensus guidelines for the management of postoperative nausea and vomiting. *Anesth Analg* 2014; **118**: 85-113 [PMID: 24356162 DOI: 10.1213/ANE.0000000000000002]

81 **Cortés-Flores AO**, Jiménez-Tornero J, Morgan-Villela G, Delgado-Gómez M, Zuloaga-Fernández Del Valle CJ, García-Rentería J, Rendón-Félix J, Fuentes-Orozco C, Macías-Amezcua MD, Ambriz-González G, Alvarez-Villaseñor AS, Urias-Valdez D, Chavez-Tostado M, Contreras-Hernández GI, González-Ojeda A. Effects of preoperative dexamethasone on postoperative pain, nausea, vomiting and respiratory function in women undergoing conservative breast surgery for cancer: Results of a controlled clinical trial. *Eur J Cancer Care (Engl)* 2018; **27** [PMID: 28474341 DOI: 10.1111/ecc.12686]

82 **Sherif L,** Hegde R, Mariswami M, Ollapally A. Validation of the Apfel scoring system for identification of High-risk patients for PONV. *Karnataka Anaesth J* 2015; **1:** 115-117 [DOI: 10.4103/2394-6954.173527]

83 **Shaikh SI**, Nagarekha D, Hegade G, Marutheesh M. Postoperative nausea and vomiting: A simple yet complex problem. *Anesth Essays Res* 2016; **10**: 388-396 [PMID: 27746521 DOI: 10.4103/0259-1162.179310]

84 **Short V**, Herbert G, Perry R, Atkinson C, Ness AR, Penfold C, Thomas S, Andersen HK, Lewis SJ. Chewing gum for postoperative recovery of gastrointestinal function. *Cochrane Database Syst Rev* 2015: CD006506 [PMID: 25914904 DOI: 10.1002/14651858.CD006506.pub3]

85 **Esnaola NF**, Cole DJ. Perioperative normothermia during major surgery: is it important? *Adv Surg* 2011; **45**: 249-263 [PMID: 21954692 DOI: 10.1016/j.yasu.2011.03.007]

86 **Sagiroglu G**, Ozturk GA, Baysal A, Turan FN. Inadvertent Perioperative Hypothermia and Important Risk Factors during Major Abdominal Surgeries. *J Coll Physicians Surg Pak* 2020; **30**: 123-128 [PMID: 32036816 DOI: 10.29271/jcpsp.2020.02.123]

87 **Journeaux M**. Peri-operative hypothermia: implications for practice. *Nurs Stand* 2013; **27**: 33-38 [PMID: 23923164 DOI: 10.7748/ns2013.07.27.45.33.e7742]

88 **Warttig S**, Alderson P, Campbell G, Smith AF. Interventions for treating inadvertent postoperative hypothermia. *Cochrane Database Syst Rev* 2014: CD009892 [PMID: 25411963 DOI: 10.1002/14651858.CD009892.pub2]

89 **Tjoakarfa C**, David V, Ko A, Hau R. Reflective Blankets Are as Effective as Forced Air Warmers in Maintaining Patient Normothermia During Hip and Knee Arthroplasty Surgery. *J Arthroplasty* 2017; **32**: 624-627 [PMID: 27546475 DOI: 10.1016/j.arth.2016.07.015]

90 **Jørgensen CC**, Jacobsen MK, Soeballe K, Hansen TB, Husted H, Kjærsgaard-Andersen P, Hansen LT, Laursen MB, Kehlet H. Thromboprophylaxis only during hospitalisation in fast-track hip and knee arthroplasty, a prospective cohort study. *BMJ Open* 2013; **3**: e003965 [PMID: 24334158 DOI: 10.1136/bmjopen-2013-003965]

91 **Petersen PB**, Kehlet H, Jørgensen CC; Lundbeck Foundation Centre for Fast-track Hip and Knee Replacement Collaborative Group. Safety of In-Hospital Only Thromboprophylaxis after Fast-Track Total Hip and Knee Arthroplasty: A Prospective Follow-Up Study in 17,582 Procedures. *Thromb Haemost* 2018; **118**: 2152-2161 [PMID: 30453352 DOI: 10.1055/s-0038-1675641]

92 **van Adrichem RA**, Nemeth B, Algra A, le Cessie S, Rosendaal FR, Schipper IB, Nelissen RGHH, Cannegieter SC; POT-KAST and POT-CAST Group. Thromboprophylaxis after Knee Arthroscopy and Lower-Leg Casting. *N Engl J Med* 2017; **376**: 515-525 [PMID: 27959702 DOI: 10.1056/NEJMoa1613303]

93 **Voigt J**, Mosier M, Darouiche R. Systematic review and meta-analysis of randomized controlled trials of antibiotics and antiseptics for preventing infection in people receiving primary total hip and knee prostheses. *Antimicrob Agents Chemother* 2015; **59**: 6696-6707 [PMID: 26259793 DOI: 10.1128/AAC.01331-15]

94 **Lamagni T**. Epidemiology and burden of prosthetic joint infections. *J Antimicrob Chemother* 2014; **69 Suppl 1**: i5-10 [PMID: 25135091 DOI: 10.1093/jac/dku247]

95 **Fsadni C,** Fsadni P. Prosthetic joint infections. *Malta Med J* 2013; **25:** 15-20

96 **Lora-Tamayo J,** Murillo O. Management of Periprosthetic Joint Infection. In Peel T (eds). Prosthetic Joint Infections. *Springer* 2018; 137-192 [DOI: 10.1007/978-3-319-65250-4\_4]

97 **Kapadia BH**, Berg RA, Daley JA, Fritz J, Bhave A, Mont MA. Periprosthetic joint infection. *Lancet* 2016; **387**: 386-394 [PMID: 26135702 DOI: 10.1016/S0140-6736(14)61798-0]

98 **Aboltins CA**, Berdal JE, Casas F, Corona PS, Cuellar D, Ferrari MC, Hendershot E, Huang W, Kuo FC, Malkani A, Reyes F, Rudelli S, Safir O, Seyler T, Tan TL, Townsend R, Tuncay I, Turner D, Winkler H, Wouthuyzen-Bakker M, Yates AJ, Zahar A. Hip and Knee Section, Prevention, Antimicrobials (Systemic): Proceedings of International Consensus on Orthopedic Infections. *J Arthroplasty* 2019; **34**: S279-S288 [PMID: 30348572 DOI: 10.1016/j.arth.2018.09.012]

99 **Liu PL**, Li DQ, Zhang YK, Lu QS, Ma L, Bao XZ, Zhang M. Effects of Unilateral Tourniquet Used in Patients Undergoing Simultaneous Bilateral Total Knee Arthroplasty. *Orthop Surg* 2017; **9**: 180-185 [PMID: 28598560 DOI: 10.1111/os.12329]

100 **Chen ZY**, Gao Y, Chen W, Li X, Zhang YZ. Is wound drainage necessary in hip arthroplasty? A meta-analysis of randomized controlled trials. *Eur J Orthop Surg Traumatol* 2014; **24**: 939-946 [PMID: 23917702 DOI: 10.1007/s00590-013-1284-0]

101 **Dennis DA**, Kittelson AJ, Yang CC, Miner TM, Kim RH, Stevens-Lapsley JE. Does Tourniquet Use in TKA Affect Recovery of Lower Extremity Strength and Function? A Randomized Trial. *Clin Orthop Relat Res* 2016; **474**: 69-77 [PMID: 26100254 DOI: 10.1007/s11999-015-4393-8]

102 **Zhang Q**, Liu L, Sun W, Gao F, Zhang Q, Cheng L, Li Z. Are closed suction drains necessary for primary total knee arthroplasty?: A systematic review and meta-analysis. *Medicine (Baltimore)* 2018; **97**: e11290 [PMID: 30045254 DOI: 10.1097/MD.0000000000011290]

103 **Yang JH**, Yoon JR, Dahuja A, Song S. Subcutaneous versus intraarticular closed suction indwelling drainage after total knee arthroplasty: A randomised control trial. *Indian J Orthop* 2016; **50**: 59-64 [PMID: 26955178 DOI: 10.4103/0019-5413.173515]

104 **Quinn M**, Bowe A, Galvin R, Dawson P, O'Byrne J. The use of postoperative suction drainage in total knee arthroplasty: a systematic review. *Int Orthop* 2015; **39**: 653-658 [PMID: 25027980 DOI: 10.1007/s00264-014-2455-2]

105 **Apfel CC**, Turan A, Souza K, Pergolizzi J, Hornuss C. Intravenous acetaminophen reduces postoperative nausea and vomiting: a systematic review and meta-analysis. *Pain* 2013; **154**: 677-689 [PMID: 23433945 DOI: 10.1016/j.pain.2012.12.025]

106 **Najafpour Z**, Godarzi Z, Arab M, Yaseri M. Risk Factors for Falls in Hospital In-Patients: A Prospective Nested Case Control Study. *Int J Health Policy Manag* 2019; **8**: 300-306 [PMID: 31204446 DOI: 10.15171/ijhpm.2019.11]

107 **Otaka Y**, Morita M, Mimura T, Uzawa M, Liu M. Establishment of an appropriate fall prevention program: A community-based study. *Geriatr Gerontol Int* 2017; **17**: 1081-1089 [PMID: 27492888 DOI: 10.1111/ggi.12831]

108 **Bayliss LE**, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, Cooper C, Carr AJ, Arden NK, Beard DJ, Price AJ. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. *Lancet* 2017; **389**: 1424-1430 [PMID: 28209371 DOI: 10.1016/S0140-6736(17)30059-4]

109 **Maradit Kremers H**, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, Jiranek WA, Berry DJ. Prevalence of Total Hip and Knee Replacement in the United States. *J Bone Joint Surg Am* 2015; **97**: 1386-1397 [PMID: 26333733 DOI: 10.2106/JBJS.N.01141]

110 **Morello RT**, Barker AL, Watts JJ, Haines T, Zavarsek SS, Hill KD, Brand C, Sherrington C, Wolfe R, Bohensky MA, Stoelwinder JU. The extra resource burden of in-hospital falls: a cost of falls study. *Med J Aust* 2015; **203**: 367 [PMID: 26510807 DOI: 10.5694/mja15.00296]

111 **Dávila Castrodad IM**, Recai TM, Abraham MM, Etcheson JI, Mohamed NS, Edalatpour A, Delanois RE. Rehabilitation protocols following total knee arthroplasty: a review of study designs and outcome measures. *Ann Transl Med* 2019; **7**: S255 [PMID: 31728379 DOI: 10.21037/atm.2019.08.15]

112 **Schache MB**, McClelland JA, Webster KE. Does the addition of hip strengthening exercises improve outcomes following total knee arthroplasty? A study protocol for a randomized trial. *BMC Musculoskelet Disord* 2016; **17**: 259 [PMID: 27295978 DOI: 10.1186/s12891-016-1104-x]

113 **Hawke LJ**, Shields N, Dowsey MM, Choong PFM, Taylor NF. Physical activity levels after hip and knee joint replacement surgery: an observational study. *Clin Rheumatol* 2019; **38**: 665-674 [PMID: 30284079 DOI: 10.1007/s10067-018-4317-6]

114 **Chua MJ**, Hart AJ, Mittal R, Harris IA, Xuan W, Naylor JM. Early mobilisation after total hip or knee arthroplasty: A multicentre prospective observational study. *PLoS One* 2017; **12**: e0179820 [PMID: 28654699 DOI: 10.1371/journal.pone.0179820]

115 **Bandholm T**, Kehlet H. Physiotherapy exercise after fast-track total hip and knee arthroplasty: time for reconsideration? *Arch Phys Med Rehabil* 2012; **93**: 1292-1294 [PMID: 22494947 DOI: 10.1016/j.apmr.2012.02.014]

116 **Saleh KJ**, Lee LW, Gandhi R, Ingersoll CD, Mahomed NN, Sheibani-Rad S, Novicoff WM, Mihalko WM. Quadriceps strength in relation to total knee arthroplasty outcomes. *Instr Course Lect* 2010; **59**: 119-130 [PMID: 20415375]

117 **Holm B**, Thorborg K, Husted H, Kehlet H, Bandholm T. Surgery-induced changes and early recovery of hip-muscle strength, leg-press power, and functional performance after fast-track total hip arthroplasty: a prospective cohort study. *PLoS One* 2013; **8**: e62109 [PMID: 23614020 DOI: 10.1371/journal.pone.0062109]

118 **Klapwijk LC**, Mathijssen NM, Van Egmond JC, Verbeek BM, Vehmeijer SB. The first 6 weeks of recovery after primary total hip arthroplasty with fast track. *Acta Orthop* 2017; **88**: 140-144 [PMID: 28079428 DOI: 10.1080/17453674.2016.1274865]

119 **Larsen K**, Hansen TB, Søballe K, Kehlet H. Patient-reported outcome after fast-track hip arthroplasty: a prospective cohort study. *Health Qual Life Outcomes* 2010; **8**: 144 [PMID: 21118517 DOI: 10.1186/1477-7525-8-144]

120 **Jones EL**, Wainwright TW, Foster JD, Smith JR, Middleton RG, Francis NK. A systematic review of patient reported outcomes and patient experience in enhanced recovery after orthopaedic surgery. *Ann R Coll Surg Engl* 2014; **96**: 89-94 [PMID: 24780662 DOI: 10.1308/003588414X13824511649571]

121 **Berg U**, Berg M, Rolfson O, Erichsen-Andersson A. Fast-track program of elective joint replacement in hip and knee-patients' experiences of the clinical pathway and care process. *J Orthop Surg Res* 2019; **14**: 186 [PMID: 31227003 DOI: 10.1186/s13018-019-1232-8]

122 **Guerra ML**, Singh PJ, Taylor NF. Early mobilization of patients who have had a hip or knee joint replacement reduces length of stay in hospital: a systematic review. *Clin Rehabil* 2015; **29**: 844-854 [PMID: 25452634 DOI: 10.1177/0269215514558641]

123 **Nussbaum EL**, Houghton P, Anthony J, Rennie S, Shay BL, Hoens AM. Neuromuscular Electrical Stimulation for Treatment of Muscle Impairment: Critical Review and Recommendations for Clinical Practice. *Physiother Can* 2017; **69**: 1-76 [PMID: 29162949 DOI: 10.3138/ptc.2015-88]

124 **Holm B**, Bandholm T, Lunn TH, Husted H, Aalund PK, Hansen TB, Kehlet H. Role of preoperative pain, muscle function, and activity level in discharge readiness after fast-track hip and knee arthroplasty. *Acta Orthop* 2014; **85**: 488-492 [PMID: 24954491 DOI: 10.3109/17453674.2014.934186]

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**Table 1 Summary of enhanced recovery after surgery pathways for oncology patients who will undergo hip or knee reconstruction surgery**

|  |  |
| --- | --- |
| **Preoperative approach** |  |
| Informed consent | Patient should be informed and consented about all the care practices he/she will receive, the expected results from his/her care, the active role he/she will have in the program and to meet all the members of the interdisciplinary team |
| Health history and determination of the patient's vital function | To determine patient’s vital function and to identify any health conditions that can be improved prior to surgery. Patient of high risk are identified by calculating individual risk based history, symptoms, health status using specific questionnaires |
| Counseling | Targeted preoperative counseling. It is recommended to quit smoking 2-4 wk and drinking alcohol 4 wk prior to surgery |
| Preoperative fasting | ERAS protocols recommend 2 h of fasting from clear fluids and 6 h of solids prior to induction of anesthesia |
| Preoperative anemia management | Preoperative anemia should be evaluated and treated before surgery |
| **Intraoperative phase** |  |
| Anesthesia protocol | Standard Anesthetic Protocol and neuraxial techniques as a part of a multimodal approach |
| GA with TIVA using continuous drip infusion of Propofol and Remifentanil is recommended by ERAS pathways |
| Neuraxial anesthesia | The gold-standard of ERAS programs is the use of epidural or spinal anesthesia, but especially for hip or knee replacement surgery is not recommended as a routine alone |
| RA/analgesia | A multimodal approach to pain management with RA and MA is supported by ERAS protocols. Should not be considered as an alternative technique to GA, but as a complement to an integrated strategy |
| Intraoperative analgesia | The use of NSAIDs or COX-2 inhibitors is recommended for the treatment of pain, in combination with paracetamol, in order to significantly reduce the use of opioid drugs in the context of a MA |
| Optimal intraoperative fluid management | Optimal fluid balance is necessary to avoid over or under hydration. Intraoperative isotonic crystalline fluids are administered to maintain the homeostasis and the electrolyte balance at a rate of 3-5 mL/kg/h |
| Prevention and treatment of perioperative nausea and vomiting | It is recommended to administer IV ondansetron 4 mg before induction to anesthesia and metoclopramide 30 min before awakening. Especially for high-risk patients, a combination of 2-3 antiemetics is recommended (ondansetron, dexamethasone, droperidol) |
| Chewing gum postoperatively appears to help mobilize the gastrointestinal system |
| Normothermia | Normal body temperature is achieved by the use of electric hot air devices (for the patient's body) and fluid warmer devices for the IV fluids or blood agents to 37-40 ℃ |
| The temperature of the operating room should not be under 21 ℃ |
| Prophylactic anticoagulant treatment | Rapid mobilization, elastic anticoagulant socks and low molecular weight heparin anticoagulant therapy for 28 d in hip surgery and 14 d in knee surgery, are recommended |
| Antimicrobial prophylaxis | The most suitable antibiotic for prophylactic antimicrobial treatment is 1st or 2nd generation cephalosporin (cefazolin or cefuroxime) intravenously 30-60 min before the skin incision, as a single-dose, depending on the patient's weight (weight-adjusted dose) |
| Surgical management | The ERAS Society makes no recommendations for surgical technique |
| However, it recommends avoiding the use of tourniquets and drains as a routine in all operations |
| **Postoperative phase** |  |
| Postoperative analgesia | Effective postoperative pain management includes a combination of analgesic drugs with central and peripheral action |
| Postoperative analgesia is determined and depends on the intraoperative analgesia plan and follows the same method used |
| The use of paracetamol 1 gr in combination with lornoxicam or celecoxib/parecoxib is recommended |
| Oral analgesia as soon as patients begins to eat |
| Postoperative fasting | Clear fluids or jelly 4-6 h post-surgery. Return to normal diet as soon as possible |
| Prevent falls after surgery | Many factors can contribute to the fall after TKA and THA, such as reoperation, elderly, female gender and comorbidities, which highlights the importance of establishing a multidisciplinary fall prevention program at every orthopedic ward |
| Physiotherapy approach | Physiotherapy, Kinessiotherapy, Strengthening |
| Physiotherapy rehabilitation of the patient undergoing TKA or THA should begin much earlier than the day of surgery, as counseling |
| After the physical evaluation, interventions are made to reduce BMI and increase muscle strength by increasing physical exercise and activity |
| The procedure can be started up to 4 wk before scheduled surgery, with regular sessions aimed at early mobilization |
| Respiratory physiotherapy with 3-flow spirometer |

ERAS:Enhanced recovery after surgery; TIVA: Total intravenous anesthesia; BMI: Body mass index; GA: General anesthesia; MA: Multimodal analgesia; NSAIDs: Nonsteroidal anti-inflammatory drugs; COX-2: Cyclooxygenase-2; TKA: Total knee arthroplasty; THA: Total hip arthroplasty; RA: Regional anesthesia.



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