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Review

Multimodal strategies to improve surgical outcome

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Abstract

Objective: To evaluate the effect of modifying perioperative care in noncardiac surgical patients on morbidity, mortality, and other outcome measures.

Background: New approaches in pain control, introduction of techniques that reduce the perioperative stress response, and the more frequent use of minimal invasive surgical access have been introduced over the past decade. The impact of these interventions, either alone or in combination, on perioperative outcome was evaluated.

Methods: We searched Medline for the period of 1980 to the present using the key terms fast track surgery, accelerated care programs, postoperative complications and preoperative patient preparation; and we examined and discussed the articles that were identified to include in this review. This information was supplemented with our own research on the mediators of the stress response in surgical patients, the use of epidural anesthesia in elective operations, and pilot studies of fast track surgical procedures using the multimodality approach.

Results: The introduction of newer approaches to perioperative care has reduced both morbidity and mortality in surgical patients. In the future, most elective operations will become day surgical procedures or require only 1 to 2 days of postoperative hospitalization. Reorganization of the perioperative team (anesthesiologists, surgeons, nurses, and physical therapists) will be essential to achieve successful fast track surgical programs.

Conclusions: Understanding perioperative pathophysiology and implementation of care regimes to reduce the stress of an operation, will continue to accelerate rehabilitation associated with decreased hospitalization and increased satisfaction and safety after discharge. Developments and improvements of multimodal interventions within the context of "fast track" surgery programs represents the major challenge for the medical professionals working to achieve a "pain and risk free" perioperative course.

Keywords: Fast track surgery; Improved outcome; Perioperative care

Surgical procedures dominate the care provided by hospitals and care centers located within the United States. In 1996, more than one half of the 71,900,000 procedures performed in this country were carried out in hospitalized patients [1]. While many of these diagnostic and therapeutic modalities were performed on acutely ill individuals who required hospitalization, a large proportion (at least 30%) were elective or semielective operations that subsequently resulted in patients remaining in the hospital for postoperative care.

Traditionally, patients have remained hospitalized after an operation in order to be observed and treated for any anesthetic or surgical complications that may arise. In addition, patients are nursed back to a level of self care before discharge. With advances in anesthetic and perioperative care and improvements in surgical technique (such as minimally invasive operations) the requirements for postoperative hospitalization have decreased. However, even with earlier discharge, patients may experience debility for several weeks or months after an operation.

Attention is now being directed toward standardizing surgical care, evaluating new therapies to be used in the perioperative period, and applying a combination of techniques to reduce complications, shorten convalescent recovery, and decrease the use of hospital resources.

This paper reviews the more contemporary evidence that relates methods of perioperative care in noncardiac surgery with shortened hospitalization and improved outcome after an elective or semi-elective operation.

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Areas for potential improvement: preoperative period

Prospective assessment of the severity of concomitant organ dysfunction is routine practice during preoperative evaluations, and appropriate care maps or recommendations are available for patients with cardiac disease [2], chronic obstructive lung disease [3], diabetes mellitus [4], and other disorders [5]. Such preoperative evaluation and optimization of organ dysfunction should be instituted in all patients to reduce morbidity and mortality.

Recent studies have shown that individuals who abuse alcohol, even in the absence of overt alcohol-related organ dysfunction, are subject to higher morbidity and prolonged recovery after an operation than nonabusers [6]. Subsequent intervention that included preoperative alcohol abstinence for 4 weeks reduced the increased morbidity after colonic surgery compared with patients who continued their drinking habits [7]. Smoking also represents a surgical risk [8]. Evaluating lung macrophage activity in patients and recent studies have demonstrated that smoking is associated with a marked reduction in phagocytic and microbicidal activity, possibly related to reduced proinflammatory cytokine activity [9]. However, no recent controlled studies have been performed to evaluate the role of preoperative smoking cessation on outcome. Efforts should be made to reduce smoking in abusers using newer modalities to aid cessation as 1 to 2 months of abstinence is required to improve pulmonary function in nonsurgical studies [10].

Preoperative nutritional support of 7 to 10 days duration is only effective in reducing complications in the more severely malnourished patients (more than 15% weight loss) [11]. However, other patient groups, such as those with Crohn's disease [12] and the elderly [13], have been found to manifest significant micronutrient deficiencies or ingest levels of vitamins and minerals below recommended allowances. Evaluation and preoperative micronutrient supplementation may be beneficial in these selected patient groups.

Practice guidelines for preoperative fasting usually recommend a 2- to 6-hour period of nothing-by-mouth before operation. Recent clinical studies have shown that preoperative intake of a carbohydrate drink may reduce the postoperative endocrine catabolic responses and improve insulin resistance [14]. Investigators have hypothesized that this approach may improve outcome. Further efficacy and safety studies are needed, however, before routine preoperative oral glucose containing drinks can be recommended.

Patient education of the postoperative care plan plays a major role in modifying the individual's response to the operative experience. Classic studies have demonstrated that the knowledgeable patient requires less analgesia in the postoperative period and at the same time, experiences significantly less pain than the less informed patient [15], and more recent investigations have supported the conclusion that preoperative information will aid coping, reduce preoperative anxiety, and may also enhance postsurgical recovery [16,17].

Operative period

Prophylactic antibiotics

Treatment immediately before the operation with a correct dose of the appropriate antibiotic is uniformly recommended for almost all operations [18]. Addition antibiotics may be indicated postoperatively with the insertion of prosthetic materials [19,20]. Timing of antibiotic administration is extremely important; intravenous infusion should occur approximately 30 minutes before the initial skin incision, thus insuring that peak tissue concentrations are achieved at the time of operation.

The tissue concentrations will generally be sustained over one half-life of the drug, and for most operations, only a single preoperative dose of drug is necessary [18]. For longer procedures not involving a prosthesis, a second dose may be indicated, but prolonged administration of postoperative antibiotics has not been associated with reduced wound infections. For colon operations, oral antibiotics are frequently used but the need for prolonged mechanical cleaning and oral antibiotics is debatable [21].

Supplemental oxygen has also been associated with a decreased infection rate [22], and the positive benefits of using this approach in the perioperative period will be reviewed later.

Use of regional anesthesia

Choice of anesthetic technique may depend on the type of surgery, preexisting disease, and effects of the agents utilized on intraoperative and postoperative organ functions. Ideally, an anesthetic technique should have extended effects on analgesia and stress-induced organ dysfunctions over the postoperative period. Regional anesthesia represents the only anesthetic technique available to date that fulfills these criteria, and regional anesthetic techniques utilizing local anesthetics are the most powerful therapy available to attenuate the endocrine-metabolic responses (the rise in cortisol, catecholamines, glucagon; hyperglycemia; insulin resistance and negative nitrogen balance) [23, 24]. This effect is most pronounced when utilized with procedures performed on the lower body where spinal or epidural anesthesia may provide a near total afferent neural blockade.

In contrast, there is a smaller inhibitory effect with thoracic epidural anesthetic techniques for operations performed in the upper abdomen [24].

The inhibitory effects on catabolic responses are most pronounced when regional anesthesia is provided for up to 24 to 48 hours, preferably as a continuous epidural analgesic technique [24]. In contrast to endocrine-metabolic re-

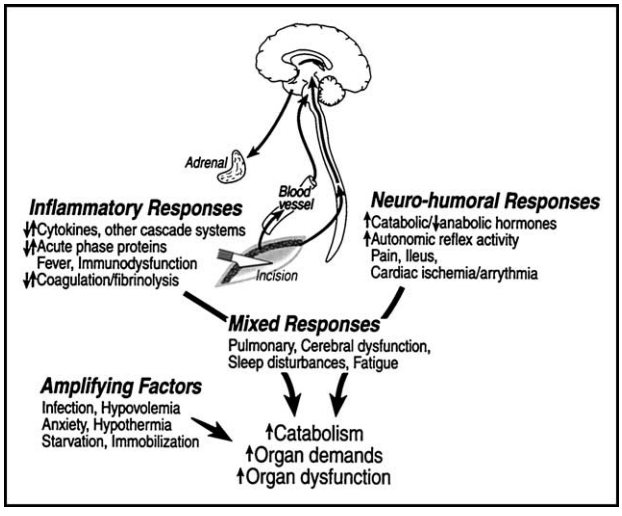

Fig. 1. Mediators and modulators of the catabolic responses after an operation. Afferent impulses from the operative site travel via the spinal cord to initiate neurohormonal responses, while local or regional inflammatory mediators are blood borne and stimulate a variety of systemic responses. Increased energy demands and accelerated net protein breakdown result in increased organ demands and organ dysfunction. Up arrows = increased; down arrows = decreased.

sponses, the inflammatory responses (alterations in concentrations of acute phase proteins, IL-6, and other cellular immune functions) are not modified by neural blockade techniques [23,24]. However, as a consequence of the reduced stress response and inhibition of autonomic reflexes that occur after an operation, postoperative organ dysfunctions may be attenuated (Fig. 1). This includes reduced impairment in pulmonary function [23,25] and decreased cardiac demands [23,26]. In addition, the ileus that accompanies intraabdominal procedures may be shortened by several days using continuous *thoracic* epidural local anesthetic with or without small doses or opioids. This effect has not been observed after *lumbar* epidural local anesthesia or epidural opioid analgesia [23,24,27,28].

Spinal or epidural anesthetic techniques may not be the first choice for many operations. For example, the intraoperative use of local infiltration anesthesia for hernia surgery provided a stress-free operation and allowed early discharge with minimal side effects [29,30]. Furthermore, urinary retention was eliminated and there was a pronounced reduction in cost. Similar results have been reported with the use of paravertebral blockade for operations on the breast [31] and with other peripheral nerve block techniques in a variety of procedures.

The use of central blockade techniques (spinal or epidural anesthesia) with or without additional general anesthesia has recently been analyzed by comparing all randomized trials with outcome from general anesthesia alone [32]. This meta-analysis demonstrates significant reduction in postoperative mortality and the rate of myocardial infarction, pneumonia, thromboembolic complications, acute renal failure, and bleeding and transfusion requirements (Table 1). No differences have been demonstrated in postoperative cerebral dysfunction between regional and general anesthesia [25,32], but none of the existing studies have altered other aspects of perioperative care, such as reducing the use of opioid and benzodiazepines and treating hypoxemia, factors that may contribute to postoperative cerebral dysfunction.

Table 1
Effect of regional anesthetic/analgesic techniques compared with general anesthesia and systemic analgesics on postoperative morbidity*

Complications	Reduction in morbidity
Pulmonary infectious complications	~30%
Respiratory depression	~40%
Pulmonary embolism	~50%
Myocardial infarction	~30%
Other thromboembolic complications	~40%
Ileus	~2 Days
Blood loss and transfusion requirements	~20–30%
Cerebral complications	No effect
Renal failure	~30%
Other infectious complications (wound, etc.)	No effect

From Kehlet [24], Ballantyre et al [25], Steinbrook [27], Halte and Kehlet [28], and Rogers et al [32].

The value of continuous epidural local anesthetic techniques in patients after procedures in the upper abdomen and thorax has been debated [23–25] although a recent meta-analysis including lower body procedures demonstrated a significant reduction of pulmonary complicatations, compared with other analgesic techniques (intercostal block, epidural or systemic opioid techniques) [25]. However, previous studies on continuous epidural analgesia have not included changes in perioperative care that incorporate earlier rehabilitation with feeding, mobilization, physiotherapy, and other approaches to be discussed later.

Minimally invasive surgery

The use of endoscopic procedures has revolutionized several aspects of surgical care and has caused major reevaluation of traditional care regimens when compared with open procedures. The use of minimal invasive abdominal surgical techniques has not resulted in a significant reduction of the classical endocrine metabolic responses, but has reduced various inflammatory responses (acute phase proteins, leukocytosis, IL-6, and so forth) and immunodysfunctions [33]. Pulmonary function has improved with less hypoxemia compared with open surgery, although differences between laparoscopic and “minicholecystectomy”are less apparent [33]. Postoperative paralytic ileus has been reduced in experimental and clinical studies [28]. Subsequently most studies have reported less pain, shorter hospital stay, and reduction of morbidity after laparoscopic surgery.

When compared with other approaches, the question remains, however, whether this is a result of altered patho-

physiological (inflammatory) responses to the operation or whether this is due to concomitant changes in postoperative care due to the expected faster recovery from laparoscopic surgery. A critical view of randomized trials comparing "open" and laparoscopic procedures indicates that traditional care regimens have rarely been revised in the open treatment groups, but have been modified in the laparascopic group, thereby favoring the expected improved outcome after minimally invasive surgery. Several studies in which hospital stay and convalescence were utilized as endpoints may merely reflect traditions of perioperative care associated with open procedures rather than differences between open and closed surgical techniques [33]. Thus, "fast track" surgery with minimal hospital stay and reduced convalescence has been reported in laparoscopic cholecystectomy, hernorrhaphy, and colonic resection. However, the same results were achieved after both open and laparoscopic procedures when the perioperative care regimens were standardized (see below).

Minimally invasive procedures will continue to be performed but the physiological and biochemical impact of these operations on outcome can only be evaluated if patients after both open and laparoscopic procedures are afforded a similar postoperative rehabilitation program designed to optimize recovery. Nevertheless, minimal invasive surgery remains one of the most important techniques for future improvement of postoperative outcome.

Intraoperative normothermia

During operations, patients are frequently subjected to cold stress, as operative rooms are maintained between 20° and 25°C, temperatures that are generally just below the zone of thermal neutrality for semiclad patients [34]. In addition, the administration of general anesthesia alters the regulatory setpoint for defense against cold exposure, thus rendering the patient poikilothermic [35]. That is, the patient's core temperature (usually 37°C) is now determined by the external environment, and hypothermia is frequently observed, particularly with moderate to prolonged procedures (longer than 2 hours). Both spinal and epidural anesthetics also alter central and peripheral thermoregulatory responses, and mild hypothermia (a reduction of 1° to 3° in core temperature) is frequently observed in patients receiving these types of regional anesthetics [35].

After operations such as aortic aneurysectomy, colectomy, or lower extremity joint replacement, it is not unusual for patients to demonstrate a falling core temperature of 2° to 4°C. This decline in central temperature stimulates the outpouring of cortisol and catecholamines and augments the stress response to the surgical procedure [36]. When compared with normothermic controls, this degree of mild hypothermia has been associated with a twofold to threefold increase in surgical wound infections [37]. In addition, hypothermia has been related to a significant increase of intraoperative blood loss, in most [38–40] but not all studies [41], an increased incidence of operative and postoperative cardiac events, including postoperative ventricular tachycardia [42,43], a 40% increase in postoperative nitrogen excretion [44], and an increase in patient discomfort [43]. Active prevention of intraoperative hypothermia by utilizing specially constructed forced air heaters placed on the operative table is recommended in major surgical procedures to facilitate recovery.

Postoperative care

Revising perioperative care regimens

Guidelines for perioperative care should be developed based upon scientific data. However, many postoperative practices have evolved from traditions that perpetuate the use of drains, tubes, catheters, and restrictions for oral intake and mobilization. These approaches have been associated in the past with a successful outcome but in light of contemporary practice may reduce recovery or even contribute to morbidity. The *routine* use of nasogastric tubes after elective abdominal surgery is unnecessary and may contribute to pulmonary complications, based upon a meta-analysis of several controlled trials [45]. The routine use of drains in cholecystectomy [46], joint replacement [47–49], colonic surgery [50,51], radical hysterectomy or lymphadenectomy [52,53], and thyroid surgery [54] does not improve outcome as determined by randomized clinical studies. Thus, routine drainage may be avoided in most cases or limited to a short period, to facilitate early mobilization. However, after mastectomy, postoperative drainage may reduce seroma formation and other wound problems [55–57]. Postoperative wound drainage after mastectomy may not limit discharge, as it can be managed on an outpatient basis.

The use of postoperative urinary bladder drainage has become routine after major operations. Few controlled studies are available to define the optimal duration of such drainage, but after major low-rectal operations, urinary bladder drainage should be limited to about 3 days and to 1 day after other types of colonic surgery [58,59]. The use of low-dose thoracic epidural bupivacaine-opioid administration for postoperative pain relief should not be an indication for bladder drainage beyond 24 hours, despite continuous epidural treatment [59].

Traditional postoperative care often includes bed rest, which is undesirable because it increases muscle loss and weakness, impairs pulmonary function and tissue oxygenation, and predisposes to thromboembolic and pulmonary complications and orthostatic intolerance [60]. All efforts should be made to enforce postoperative mobilization, which is possible with effective pain relief.

Oral intake is frequently limited in the postoperative period. When enteral feedings are provided, they are often given as a diet progression from liquids to soft to solid food;

there is no scientific basis for such practice. In fact, several studies have shown that early oral feedings are safe even after colonic surgery with bowel anastomoses [61–63]. If nausea, vomiting, or ileus are present, effective pharmacological treatment should be utilized and feeding should be initiated.

Thromboembolic prophylaxis

Surgical injury changes the coagulatory/fibrinolytic balance in favor of coagulation, thereby increasing the risk of deep venous and pulmonary thromboembolism. Guidelines for prevention of venous thromboembolism have therefore been developed based upon numerous randomized trials and meta-analyses [64]. However, such guidelines have rarely considered the role of anesthetic-analgesic techniques in prophylaxis. A recent meta-analysis [32] and review [65] have emphasized the important role of epidural analgesia to reduce deep venous thrombosis and pulmonary embolism even in high-risk patients undergoing major joint replacements. Preliminary observations suggest that combined treatment with epidural analgesia and chemoprophylaxis may further reduce thromboembolism [65]. Unfortunately, in the United States low molecular-weight heparin has been administered at a higher dose than given in Europe, resulting in an apparent higher risk of epidural hematoma. The combined use of neuraxial block and standard heparin thromboembolic phrophylaxis does not carry increased risk [66], but combined use of neuraxial block and low molecular-weight heparin with doses recommended in the United States require more study, with doses adjusted downward to meet revised practice guidelines [67].

The use of intermittent pneumatic compression is widespread owing to the documented efficacy [64] and avoidance of potential hemorrhagic complications. However, pneumatic compression devices may limit early mobilization, which otherwise is considered to be of major importance to prevent postoperative thromboembolism.

Pain control

Despite much progess in our understanding of pain physiology [68] and attention from professional and government agencies [69,70], routine postoperative pain management usually remains unsatisfactory [71]. This is unfortunate, since well-established treatment regimens are available [72, 73], and the implementation of such programs with the introduction of acute pain services improves quality of care [69,70]. Furthermore, sufficient pain relief is a prerequisite for optimal recovery [74].

Effective treatment of postoperative pain that allows for early mobilization, may be achieved using a combination of analgesic agents or techniques (balanced analgesia) [73]. The concept of multimodal or balanced analgesia takes advantage of the additive or synergistic effects by combining multiple agents. Moreover, with several combination regimens there is concomitant reduction of side effects owing to the lower doses of the individual drugs and differences between drugs in side effect profiles [73].

The use of simple and safe local anesthetic infiltration techniques in small operations should be emphasized [75], and the use of continuous epidural techniques for more severe pain is well established [23,73]. Early mobilization after major procedures can only effectively be accomplished by utilizing epidural or other local anesthetic techniques rather than with opioids, nonsteroidal anti-inflammatory drugs (NSAID), or other systemic analgesics. However, the concept of opioid-free or opioid-reduced analgesia should receive further attention in the future, as reduction of opioid-related side effects may hasten recovery [76]

Antinausea prophylaxis

Postoperative nausea and vomiting are among the most common postoperative complaints and these problems are an inconvenience and may limit recovery and hospital discharge.

Predictive factors for nausea include a previous history of motion sickness and postoperative vomiting, anxiety, type of surgical procedure (increased risk during head and neck surgery), dehydration, and female sex [77]. In recent years, well-designed controlled trials have demonstrated significant antinausea and vomiting effects of proprofol anesthesia [78] and ondansetron (or other similar drugs) [79]. Moreover, nausea and vomiting were reduced with the omission of nitrous oxide [80]. A single dose of dexamethasone given preoperatively reduces nausea and vomiting in minor to moderate sized operations [81]. Droperidol is also effective [82]. Finally a recent study suggests that intraoperative and early postoperative supplemental oxygen may reduce nausea and vomiting after colonic surgery [83], and the effects may be as effective as ondansetron [84].

Local anesthesia may provide effective postoperative pain relief, thereby reducing use of systemic opioid and indirectly reducing nausea and vomiting [85–87]. Because the technique of continuous epidural local anesthesia reduces the need for systemic opioids, this technique will also reduce nausea and vomiting as oral intake is possible (see below). The use of NSAID's to provide early postoperative analgesia and a 20% to 30% opioid-sparing effect may reduce nausea and vomiting but further studies are needed [76,88]. Several other pharmacological agents (phenothiazines, antihistaminics, anticholinergics, and benzamides) may exhibit some antinausea and vomiting effects, but the efficacy of these drugs is less well-established. Metoclopramide is ineffective [89]. Future effective control of nausea and vomiting probably require multimodal intervention, but data are not available at this time to allow recommendation for such combinations [90–92].

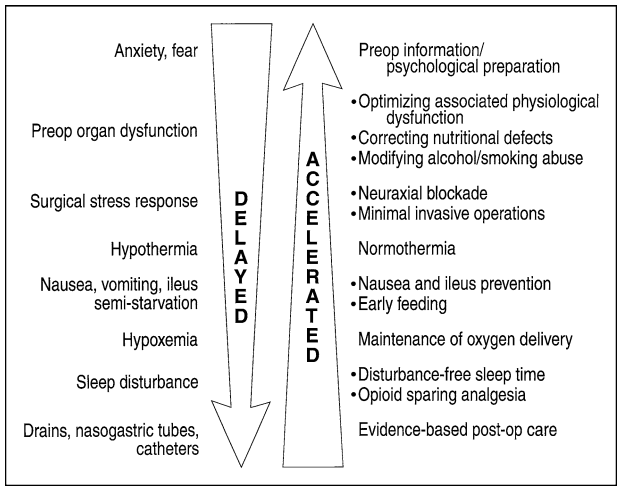

Fig. 2. Factors that contribute to delayed or accelerated recovery after elective operations.

Early enteral nutrition

Traditional care regimens after major operations have usually included restricted oral intake, which contributes to catabolism with loss of weight and skeletal muscle. Several experimental and clinical studies have demonstrated that early enteral nutrition reduces gut permeability (and presumed bacterial translocation) when compared with parenteral nutrition or late enteral feeding. Some authors suggest that early enteral feeding may reduce infectious complications and improve outcomes [93,94]. However, several of these studies have been performed in patients after accidental injury [93] and the exact role of routine early enteral tube feeding [95,96] or feeding with oral dietary supplements after elective procedures remains controversial. In recent years, more well-described but small studies have been performed to suggest that early enteral nutrition is possible and may be valuable even in selective elective surgical patients [61,97,98]. Although theoretically promising, specific nutrient pharmacotherapy utilizing immune-enhancing nutrition also needs further study before this can be recommended for routine use, since consistent benefits have not been found [95,99-102]. Future improvement in perioperative care with effective treatment of nausea, vomiting, and ileus (see above), may allow early enteral (oral) nutrition to become routine therapy thereby reducing catabolism and limiting loss of muscle function and postoperative fatigue. Future studies with appropriate analgesic techniques to reduce ileus [28] need to be performed in order to reevaluate the role of enteral nutrition on morbidity.

Single factor intervention with additional protein-enriched supplements for 10 to 16 weeks after discharge after abdominal surgery has increased body weight and lean body mass [103] while the effect on recovery, hand grip strength, and quality of life could only be demonstrated in depleted patients [103,104]. These findings suggest that prolonged nutritional therapy has no major benefit except in depleted patients.

Postoperative hypoxemia

Postoperative hypoxemia may occur in the early recovery period as a consequence of anesthesia-related effects, and as a late event during the days when the patient is receiving less acute care [105]. The late postoperative hypoxemia may occur as a persistent phenomenon or as episodic desaturations, usually occurring at night [106]

The constant hypoxemic response is closely related to the conventional impairment in pulmonary function and supine position [107] while episodic desaturations are predominantly related to postoperative sleep disturbances with rebound of REM-sleep during the second to fourth postoperative night [105,106]. Late postoperative hypoxemia has been identified as an important contributing factor to postoperative cardiac dysfunction (ischemia and arrhythmias) and possibly to myocardial infarction [105]. Decreased tissue oxygen tension may also play an important role in wound infection and delayed wound healing as well as disturbances of cognitive function [105]. Modification of the usual hypoxemic responses should focus on techniques to improve postoperative pulmonary function and sleep, or to provide supplemental oxygen. Postoperative pulmonary function can be improved by providing sufficient analgesia, where continuous epidural analgesia with local anesthetics is most effective. The position of the patient is important, since the usual supine position during the postoperative period may impair pulmonary function and further reduce oxygen saturation, while mobilization improves pulmonary function and oxygenation [106]. Postoperative sleep disturbances and episodic desaturations may be improved by sufficient analgesia with regional local anesthetic techniques and reduced use of opioids, which may contribute to sleep disturbances [105,108]

Oxygen administration increases oxygen delivery, but has no effect on the incidence of episodic desaturations [105]. However, early postoperative oxygen administration may reduce nausea and vomiting [83] decrease the incidence of surgical wound infection [109], and reduce tachycardia [110]. Furthermore, cerebral dysfunction may be improved [105]. Although no controlled data are available from the late postoperative period, routine oxygen administration is indicated in high-risk patients for the first 2-4 days when patients are in the supine position (night time) or when oxygen saturation is less than about 93%.

Convalescence

Postoperative convalescence may depend on several factors of which pain, fatigue, rehabilitation, and specific surgical factors are most important [111]. Early postoperative fatigue may be related to distorted sleep resulting from noise, drugs (opioids, benodiazepines), and the inflamma-

Table 2
Results from fast track programs compared with traditional care in the United States

Type of operation	Postoperative hospitalization		Comments and other findings
	Fast track	Traditional*	
Inguinal hernia repair [29,30]	2–7 hours	Ambulatory or 1 day	Large consecutive patient series, fast track surgery utilized local infiltration anesthesia in > 95%, documented low morbidity, no urinary retention. Cost reduction> $250 procedure with local anesthesia compared with other types of anesthesia. Patient satisfaction ~90%.
Cholecystectomy			
Laparoscopic [122–124]	>90% discharged on same day	1–2 days	Large consecutive patient series, documented safety, patient satisfaction >90%. Randomized study [124] documented cost reduction $750/patient.
Mini incision [125]			Large consecutive patient series, safety documented.
Fundoplication [126]	<1 day	2–3 days	Selected low-risk patients (n = 45).
Colorectal resection			
Open [63]	2–3 days	8–11 days	Preliminary studies (n = 60) including high-risk patients. Cardiopulmonary morbidity reduced.
Laparoscopic [127]	2–3 days	4–6 days	High-risk patients (~80 yrs; n = 50). Results as with "open" fast track series.
Lung resection [128]	1 day	8–10 days	Preliminary study (n = 10).
Carotid endarterectomy [129–131]	90% <1 day	3–4 days	Surgery under local anesthesia, nurse and ward specialization.
Abdominal aortic aneurysmectomy [132]	3 days	7–10 days	Preliminary study (n = 50).
Lower extremity arterial bypass [133]	2–3 days	6–9 days	N = 130, safety documented.
Radical prostatectomy [134]	1–2 days	4–5 days	Preliminary study (n = 100), patient satisfaction > 95%.
Mastectomy [135–137]	90% <1 day	2–3 days	Cumulated large patient series. Documented safety [135,136], major cost reduction, high patient satisfaction > 90%. Randomized study: no increased morbidity with fast track, but less wound pain and improved arm movement; no increased risk of psychosocial complications [137].
Adrenalectomy [138]	<1 day	3–5 days	Preliminary study (n = 9).
Donor nephrectomy [139]	<1 day	3–7 days	Preliminary study (n = 41).

* These data are derived from a hospital data base [121] and large multicenter trials published over the last 5 years. These lengths of stay are generally reflective of the current level of care in the United States.

tory response (IL-6) [111,112]. Late (weeks) fatigue is related to loss of weight and muscle mass and associated weakness [111,113].

Postoperative pain can be effectively treated with multimodal analgesia thereby allowing early mobilization (see above), and fatigue may be reduced by combined inhibition of the catabolic response with neural blockade techniques, early nutrition, and mobilization [111]. These approaches appear to be the most important factors to enhance convalescent recovery.

Recommendations for care during the convalescent period are highly variable [114] and this period of care is rarely studied. There seems to be no scientific basis for restrictions of activities of daily living. Studies in animals showed a resumption of strenuous physical activity (greyhound racing) 2 weeks after an abdominal procedure with no deleterious effects [115] whereas convalescence in patients frequently averages 4 to 5 weeks [116]. Although no controlled data are available, large, single-center studies of hernia surgery have shown that recommendations for immediate activity may shorten convalescence to about a week after inguinal herniorrhaphy [30,117] in contrast to 2 to 4 weeks after laparoscopic repair or open herniorrhaphy with traditional recommendations to limit postoperative activity [118]. Such recommendations regarding convalescence should be reviewed and adjusted as information based on clinical trials become available.

Interrupting preoperative medications

Recent observations suggest that an increased incidence of cerebrovascular complications may occur in the postoperative period with cessation of chronically used appropriate medication after the operation [119]. This especially applies to agents such as beta-blockers, antihypertensives, angiotension converting enzyme inhibitors, benzodiazopams, and antidepressives. These agents should therefore be continued in the postoperative period.

Potential of multimodality therapy

The risks and morbidity associated with surgical procedures may be determined by multiple factors (Fig. 2). Although improvement in operative outcome has been achieved due to single interventions such as antimicrobial prophylaxis or antithrombotic therapy, further major reduction in morbidity using single intervention approaches may

Table 3
Organizational steps necessary to develop a fast track surgical program

Step	Personnel involved	Specific task/estimated Time required, if applicable	Comments
1. Develop a plan or critical pathway.	All individuals who interface with the patient	Write a pathway to be followed. Meetings lasting 1–2 hours a week for 1–2 months.	Leader needed with skills in consensus development, knowledge in process engineering. Identify team members committed to project.
2. Outline specifics of preoperative preparation.	1° Surgeon 2° Consulting internist	Evaluate need for tests and preventive strategy to optimize physiology (~25 hours).	Emphasis on minimizing comorbid condition such as heart disease, pulmonary disease, diabetes mellitus, and thromboembolic and infection risk.
3. Develop anesthesia and analgesia programs.	1° Anesthesiologists/pain service 2° Surgeons, nurses	Optimize regional techniques to reduce the stress response and optimize pain management. Initiation and development of program may require 2–3 months.	May require special training for anesthesiologists to perform epidural and other neural block techniques. Nurses may profit by visiting units with protocols in place to maintain patients pain free for the early postoperative period.
4. Minimize stress of operation.	1° Anesthesiologist/surgeon 2° Operating room and recovery room nurses	Optimize anesthetic technique. Practice minimal invasive surgery. Prevent perioperative hypothermia. Minimize transfusion requirements.	
5. Adjust postoperative care according to evidence-based studies.	1° Surgeon 2° Nursing staff	Modify practice regarding drains, tubes, catheters, etc. Have standard protocols for feeding and ambulation.	Standardize postoperative orders. Staff may profit by a visit to a center practicing fast track surgery.
6. Develop postoperative nursing care programs.	1° Nurses, nursing assistant 2° Physiotherapists, dieticians	Enforce feeding, ambulation, and sleeping protocols.	Staff may benefit by visiting to a center already practicing fast track surgery.
7. Determine patient follow-up.	1° Surgeon 2° Nurse practitioner, surgical assistant	Provide a system for telephone follow-up and office visit by senior members of the team.	Protocols should be developed for specific and rapid responses to pain, nausea and vomiting, wound drainage, and other complaints that traditionally require readmission.
8. Develop a patient information program.	All team members, possibly headed by a nurse practitioner or patient educator.	Develop oral, written, and video material to educate patient before the operation.	
9. Document results, tabulate problems and patient satisfaction. Revise and improve program.	All team members, possibly headed by a data manager.	Develop outcome measures and methods of follow-up.	May require specific training in outcome research.

Fast track recommendation for specific procedures are found in the references cited in Table 2. 1° = primary personnel; 2° = secondary personnel.

not be possible. Additional improvement in postoperative outcomes may therefore require more attention by combining efforts from anesthesiologists and surgeons in the intraoperative and early postoperative period (1 to 4 days), where the peak incidence of complications occur.

A rational approach towards control of postoperative pathophysiology and morbidity may therefore be multimodal intervention [120]. Such efforts represent an extension of conventional "clinical pathways," because they integrate recent data from pain physiology and treatment, anesthesia, surgical technique, enforced feeding and mobilization, and revision of traditional care programs into an effective postoperative rehabilitation program. The terminology for such programs has included such expressions as "fast track" or "accelerated recovery programs."

In recent years, several reports describing fast track programs have been published (Table 2). A common feature of these reports is a reduction of hospital stay with low morbidity. Most available data are small-scale nonrandomized patient series from single centers.

Therefore, the suggestions from these studies of reduction of hospital stay, organ dysfunction, and morbidity need further assessment with a focus on patient safety after early discharge. In addition, a detailed cost analysis should be performed including the potential for extra costs resulting from readmissions and the need for rehabilitation services or care provided by home nursing. However, from the few randomized trials available patient safety and satisfaction have been preserved [123,137,140] and cost reduced [124, 141] compared with traditional postoperative stay pro-

grams. In addition, pharmacological, sympathetic blockade that reduces cardiac demands and mortality, will probably be utilized to enhance outcome in the future [142,143].

A prerequisite for an "accelerated recovery program" is a multidisciplinary collaboration that requires organization to successfully interface between the patient, the surgeon, the anesthesiologist, physiotherapist, and surgical nurse (Table 3). Such programs therefore represent an expansion of the function of the more traditional acute pain service. Other characteristics of the programs are nurse specialization, direction of patients after specific operations to assigned areas of care (ie, specialized units), optimal use of regional anesthetic techniques and balanced analgesia, opioid-free or opioid-reduced analgesia, and a willingness to reconsider and revise the use and necessity of traditional postoperative care principles (drains, tubes, catheters, restrictions, and so forth).

It should be emphasized that accelerated recovery and fast track surgical programs are based on the concept that multimodal intervention may reduce stress induced organ dysfunction and the accompanying morbidity that results in the subsequent need for hospitalization. This may have major social economic implications, in contrast to the effects of modifying only one single factor (hospital stay), which may have minimal impacts on overall costs [144].

In summary, recent developments in the understanding of perioperative pathophysiology and the implementation of care regimens to attenuate the stress of an operation, suggest that a comprehensive revision of postoperative care towards accelerated rehabilitation may decrease morbidity and the need for hospitalization with increased satisfaction and safety after discharge. Development and improvement of multimodal intervention within the context of fast track surgery programs represent the major challenge for the medical professions working to achieve a pain and risk free perioperative course.

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