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Enhanced recovery after surgery

From clinical observations to evidence-based practice

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ABSTRACT

Enhanced recovery after surgery was developed based on the question "Why is the patient in hospital?" and is evolving in the context of multimodal perioperative care programmes with documented major benefits with respect to the need for hospitalisation and the risk of complications. Despite being a worldwide success, future challenges to improvements include patient and procedure-specific modification of inflammatory/immunological stress responses, improvement of post-discharge recovery, closing the knowing-doing gap between scientific evidence and clinical practice, and improving research design strategies.

KEY POINTS

- Enhanced surgical recovery programmes have reduced the need for hospitalisation and the risk of complications.
- Improvements are required including in post-discharge recovery.
- The research focus is on surgical stress response modification based on patient and procedure-specific data.
- Implementation of scientific evidence remains a challenge.

Despite major progress in perioperative care, the risk of post-operative complications, delayed recovery and death remains substantial. Interestingly, the initial hypothesis by George Crile in 1913 on "anoci-association" introduced the idea that blocking afferent neural input to the central nervous system might prevent post-injury organ dysfunction [1]. However, this fascinating hypothesis had limited initial clinical consequences. Over the years, the concept of "stress-free anaesthesia and surgery" was developed further [2]. However, it was rapidly recognised that the pathophysiological changes to injury were more complex and not limited to affecting the central nervous system. Thus, attention has been dedicated to the specific role of pain, fluid and blood management, reduction of the inflammatory/immunological surgical stress responses by minimal invasive surgical techniques and revision of traditional surgical care principles with unnecessary use of nasogastric tubes, drains, catheters and functional restrictions. Consequently, in 1997 and based on initial small observational studies in colonic surgery [3], the concept of "fast-track" or "enhanced recovery" surgery was developed as a multimodal effort to reduce the need for hospitalisation and limit complications [4, 5]. This article is a short, updated narrative review based on personal views of the history, the current status and future challenges for improvement of the concept.

THE CONCEPT AND INITIAL OBSERVATIONAL STUDIES

Although early efforts were made in fast-track cardiac anaesthesia, including early extubation and the development of minor ambulatory procedures, the initial breakthrough was the observation that a multimodal effort with combined use of regional anaesthesia, multimodal analgesia, early ambulation and feeding reduced the hospitalisation period from the international 10-14-day standard to 2-3 days in elderly patients undergoing colonic resection [3, 6]. Subsequently, these non-randomised clinical observational studies have been confirmed worldwide, including in randomised controlled trials; and the concept is now accepted globally to represent value-based care. Subsequently, these observations have been extended to almost all surgical procedures such as major urology, gynaecology, thoracic procedures, orthopaedic surgery, major breast procedures, etc. [7]. Based upon the results, several international "enhanced recovery after surgery" (ERAS) societies have been formed of which the "ERAS Society" has been one of more prominent [8, 9]. However, despite this success, challenges still exist for further development and improvement of the concept; major procedures are still risky, an increasing number of patients has preoperative multiorgan comorbidity and the elderly surgical population is increasing [7].

CHALLENGES FOR IMPROVEMENT

Due to the multifactorial nature of surgical risk, the challenges need to focus on specific pathophysiological and on organisational risk factors as listed in **Table 1** and then to integrate them into a procedure and patient-specific package in clinical practice. The basic mechanism of surgical risk is the multifaceted surgical stress responses among which the inflammatory/immunological responses are receiving more attention and were demonstrated to play a major role for recovery [10]. Thus, the classic hormonal catabolic responses are less important in established fast-track programmes owing to the use of multimodal analgesia, early oral feeding and mobilisation [11]. Importantly, modification of the inflammatory responses must be balanced against a focus on "high-inflammatory" responders [10]. Presently, the use of minimal invasive surgery and preoperative use of high-dose steroids seems most promising [12-15], but requires optimisation including new patient and procedure-specific approaches [11].

TABLE 1 Pathophysiological and organisational challenges to future improvements of enhanced recovery after surgery.

Pathophysiological challenges
Prehabilitation
Surgical stress responses
Minimal invasive surgery
Pain management
Fluid management
Blood management
Thromboembolic complications
Cognitive dysfunction and "psychiatric" issues
Orthostatic intolerance
Emergency procedures
Organisational challenges
The knowing-doing gap
Guidelines
Outcome assessment
Research strategy

Obviously, optimal pain management allowing early mobilisation is a prerequisite to a successfully enhanced recovery programme in which the multimodal opioid-sparing approach [16] is well accepted. However, despite the success, the concept requires more studies on a procedure and patient-specific approach including "high-pain responders" [17, 18]. Importantly, the future focus must include the post-discharge recovery period for which the number of pain studies conducted is limited compared with studies focusing on the early in-hospital period.

Although not included in the initial programmes, the concept of "blood management" has been demonstrated to be important and has been separated into the preoperative phase with a need for anaemia diagnosis and treatment, intraoperative reduction of blood loss with tranexamic acid and minimal invasive surgery [19]. However, a need exists for post-operative anaemia studies to elucidate the haemoglobin threshold for optimal functional recovery.

Post-operative cognitive dysfunction is again well-recognised as a multimodal problem including the inflammatory responses, pain, opioid use, sleep disturbances and specific neuroinflammatory responses [20, 21]. Unfortunately, most cognitive dysfunction studies have focused on single interventions without considering the concept of enhanced recovery [22]. In contrast, future studies should include a fully implemented enhanced recovery programme before studying specific interventions.

Thromboembolic complications are a paradox response to an otherwise successful anaesthetic and surgical procedure, and immobilisation is probably the most important risk factor. Consequently, enhanced recovery programmes with early mobilisation carry a reduced thromboembolic risk [23] and have reduced the need for potent anticoagulation prophylaxis. However, more disease-specific studies are required in certain high-risk

patients (cancer, etc.).

As early mobilisation is a key component of enhanced recovery programmes, early orthostatic intolerance [24] represents another pathophysiological challenge. In this context, autonomic nervous system dysfunction and use of opioids are important. Again, further patient and procedure-specific studies are required since anaesthesia *per se* may not be important as even a prolonged superficial procedure like breast cancer surgery with general anaesthesia was not followed by relevant orthostatic intolerance [24]. Improved preoperative characterisation of the autonomic nervous system function by heart rate variability assessment may be an important future topic for risk assessment and improvement [25].

From the very beginning, it was obvious that fluid management should receive a strong focus since even in minor procedures, too little or too much fluid may delay early recovery and limit a successful outpatient procedure [26]. A considerable number of studies have focused on the type and amount of fluids needed, including a specific focus on goal-directed management (for example in the form of optimisation of cardiac stroke volume). Miller summarised that balanced solutions should be used and will work well at a 1.0-1.5 l positive fluid balance in conjunction with stroke volume optimisation [27]. However, more research is required in the form of fully implemented enhanced recovery studies, especially regarding the later post-operative period in the surgical ward. Another challenge is the role of vasopressors [28] and development of techniques for tissue perfusion assessment on an organ-specific basis to guide proper fluid management.

More recently, attention has been given to exploring psychiatric diseases as a surgical risk factor, but where recent data have suggested that it is most probably the psychopharmacological treatment *per se* that is important rather than the psychiatric diagnosis as such [29].

Another challenge is to develop clinically relevant ERAS programmes for emergency procedures (i.e. abdominal, hip fracture, etc.). Here, initial observations are positive but need to focus on the later post-anaesthesia/surgery period and overall post-operative surgical care aspects based on the knowledge obtained from elective procedures [30].

Since more patients are elderly and have pre-existing comorbidities, the concept of prehabilitation has been developed, producing various initial, promising results [31]. However, the data have been somewhat disappointing [32], probably because they have not included the really high-risk patients or comprised a fully implemented ERAS programme explored in combination with a rational prehabilitation programme [33].

In addition to the many pathophysiological factors to be considered for improvement, organisational issues remain such as closing the knowing-doing gap since there is still insufficient implementation of the well-documented scientific data on ERAS programmes [34, 35]. In this context, a stronger focus is required on the institutional basis - including anaesthesiologists, surgeons, nurses and physiotherapists monitoring their own data and then comparing their findings with the enhanced recovery literature followed by implementation of well-documented programmes. Such efforts have been proven very successful on a regional basis in Canada [36] and have demonstrated the importance of leadership at a high organisational level. One cause of the implementation problem may be that the published ERAS guidelines [8, 9] are usually very complicated and include up to more than 30 factors. Thus, initially successful programmes were achieved simply based on a limited number of the more relevant factors [37-40].

Importantly, future improvements will depend on the multi-professional approach, since single-type interventions, even those adopting rational approaches such as minimal invasive surgery (laparoscopy or robots), must be integrated into ERAS programmes to underpin and document the benefits, as discussed in colonic resection [6] and bladder cancer cystectomy [41].

Recently, the debate on outcome assessment has intensified with improved objective assessment of complications such as Dindo-Clavien scoring or the Combined Complication Score (CCI) [42]. Another important outcome issue is "objective" assessment of functional recovery by new wearable technologies [43] versus the popular "patient-reported outcomes" (PRO). For this author, the primary challenge remains to clarify the question "Why in hospital?" or "Why not returning to normal function?", which must include an objective documentation of function combined with PRO to evaluate the reasons for delayed subjective patient-reported recovery. Here, much research needs to be done, since disappointing "objective" outcomes may run contrary to more positive PRO [44]. Another post-operative outcome assessment method used has been the concept of "days alive and out of hospital" (DAOH), which is very relevant from a patient view and also from a healthcare economic view as it demonstrates daily life consequences during recovery in a given period. So far, results of major interest have been reported from several procedures, including total hip and knee arthroplasty [45], lung cancer [46] and bladder cancer surgery [41]. These results have shown the healthcare burden to be more complex as the outcome may not depend only on the early postsurgical enhanced recovery period (0-30 days). Rather, the subsequent up to one-year period may depend on disease-specific factors, adjuvant therapy, etc. Such data are relevant for the overall interpretation of the outcome and indication for the surgical intervention.

Finally, despite the extremely positive data from ERAS programmes underpinning the feasibility of even outpatient procedures in hip and knee arthroplasty, lung cancer surgery, kidney cancer, colonic surgery and many other procedures, the question remains whether these preliminary data have more general implications [47]? Thus, it must be emphasised that the aim of ERAS is not only to enhance speed of recovery and reduce hospital stay, but primarily to achieve and enhance safety, i.e. "first better – then faster".

In summary, the concept of ERAS represents a global success in value-based healthcare, but several challenges exist for further improvement towards the goal of achieving a "pain and risk-free" operation. From a scientific design perspective, it is interesting that the concept was developed and documented based on simple detailed cohort studies and not on randomised clinical studies – although these have subsequently confirmed the value of the concept. Due to the multifactorial nature of post-operative recovery, future scientific documentation efforts need to consider the often-negative findings in perioperative medicine from large pragmatic randomised clinical trials without documented ERAS implementation versus results from detailed single or multicentre procedure and patient-specific cohort studies combined with a fully implemented evidence-based ERAS programme [47]. To this author, a fully implemented ERAS programme is a prerequisite to considering a large randomised controlled trial [47]. This discussion is highly relevant to enhancing progress considering the cost differences between these research design strategies and the chance of success.

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