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REVIEW ARTICLE

Intraoperative Factors Influencing Postoperative Outcomes in Older Patients Undergoing Abdominal Surgery—Narrative Review

Kinga Mastalerz[1] · Jakub Kenig[1] · Urszula Skorus[2]

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Abstract
The population of Europe is growing and ageing. Therefore, the number of elderly patients requiring surgical intervention is expected to rise markedly in future years. There has been considerable research into the influence of preoperative patient and disease factors on postoperative outcomes. However, information regarding the relationship between intraoperative factors, and postoperative morbidity and mortality in older patients is lacking. We aimed to review the literature concerning intraoperative factors that impact on postoperative outcomes in elderly patients. PubMed, Scopus and Embase databases (January 2006 to December 2017) were searched using the keywords of "postoperative mortality" OR "postoperative morbidity" AND elderly OR older. Fifty studies were identified for inclusion in this review. Many intraoperative factors have been identified that contribute to the extent of an individual's reaction to a strong stimulus such as surgery. Some of these are modifiable (e.g. procedure duration, surgical method, experience of the surgeon and anaesthetist, blood loss and hypothermia) while others are not (e.g. mode of surgery and location of surgical procedure). There is a distinct lack of research on postoperative morbidity and mortality in elderly patients, especially in those with frailty syndrome. The elderly are not simply "older adults" and extrapolation of study findings from a younger population may carry a high risk of error. Therefore, further well-designed studies are needed in elderly patients, especially in those with frailty syndrome. The latter being most exposed to perioperative complications, longer hospital stays, readmissions and mortality.

Keywords Elderly · Frailty · Surgery impact · Surgical Apgar Score

Introduction

The population of Europe is growing and ageing. It is predicted that by the year 2020, elderly people will outnumber children younger than 5 years of age for the first time in history. By the early 2030s, over one third of Europe's population will be at least 65 year of age, and the number of individuals who are at least 80 years of age will double. Therefore, it can be expected that the number of elderly patients requiring surgical intervention will rise markedly in the years to come.

Both the surgery and its associated procedures such as vascular and urinary catheter placement, intubation, and general or spinal anaesthesia lead to local tissue damage, compromised natural barriers and exposure to external factors (physical, chemical and microbiological). Together, these incite an array of physiological changes involving neuroendocrine, cytokine-immunological, hydro-electrolyte and metabolic systems. Elderly patients already have reduced physiological reserves and age-related comorbidities that augment perioperative stress. This may lead to exhaustion of the body's compensation capabilities, multiorgan failure and death. This is a particular concern for people with the frailty syndrome.

Research into the influence of preoperative patient and disease factors on postoperative outcomes has been the subject of many studies [1]. However, there is scare literature regarding the relationship between intraoperative factors, and postoperative morbidity and mortality. The aim of this work was to review the recent literature concerning intraoperative factors that affect postoperative outcomes in older patients.

✉ Kinga Mastalerz
kingammastalerz@gmail.com

[1] Department of General, Oncological and Geriatric Surgery, Jagiellonian University Medical College, Krakow, Poland

[2] Jagiellonian University Medical College, Krakow, Poland

Material and Methods

In January 2018, a literature review was conducted using studies published in PubMed, Scopus and Embase databases between January 2006 and December 2017. The search strategy used was "postoperative mortality" OR "postoperative morbidity" AND elderly OR older. Study selection was based on review of the titles, abstracts and articles, which ultimately resulted in 50 papers meeting our inclusion criteria:

- Type of research: all research types published in English, German, Spanish and French.
- Study participants: all patients were at least 65 years of age. Where no published research was available, studies concerning elderly people without particular age grouping were included.
- Type of procedure: all procedures except for those from the fields of orthopaedics, trauma and neurosurgery.

Results

The intraoperative factors that were identified as influencing the magnitude of an individual's response to perioperative trauma were as follows: location and extent of surgery, duration of surgery, intraoperative blood loss, method and type of surgery, anaesthesia type, hypothermia, and surgeon and anaesthetist experience [1–52].

Location and extent of surgery is one of the most important factors influencing postoperative outcome. Older patients undergoing low-risk surgeries such as thyroid resection, or parathyroid or inguinal hernia surgery under spinal anaesthesia, do not have significant differences in short- or long-term results compared with a younger population [2–4]. For open or minimally invasive procedures of the gastrointestinal tract, non-selected elderly patients have a higher postoperative complication and death rate, than younger people. Discrepancies in these outcomes last 6 to 18 months post-procedure, depending on the publication [5–7]. Beyond this period, older and younger people have similar outcomes provided that the procedure was undertaken with the intent to cure. A third group of procedures have significantly worse results in the elderly if the surgery was not conducted in a highly experienced centre. These procedures include pancreatic and liver surgeries. Thus, preoperative evaluation must include appropriate selection of patients for high-risk procedures. While these studies provide some insight into the influence of location and extent of surgery on outcomes in elderly patients, high-quality research in patients with frailty syndrome is lacking [8, 9].

There were only a couple of publications on *surgery duration*, and their conclusions were contradictory. Many factors influence the duration of surgery. On the one hand, these include procedure complexity, operating method, experience of the surgical team and occurrence of intraoperative complications. On the other hand, there might be a deliberate action aimed at avoiding errors. Jackson et al. analysed over 76,000 laparoscopic surgeries and showed a statistically significant increase in the complication rate with the lengthening of certain procedures (laparoscopic removal of colon or gallbladder, and fundoplication). This tendency was not confirmed with inguinal hernia repair procedures. No publications focused on the elderly were identified [10, 11].

Blood loss and transfusions of blood-derived products cause ejection of inflammatory mediators. This mechanism is likely responsible for poorer results when treating elderly patients needing transfusions after trauma and surgery. Researchers do not agree as to what volume of intraoperative blood loss importantly impairs an individual's haemodynamics and cellular metabolism to effectively force treatment with fluids or blood products. Both Mastracci et al. and Wu et al. [12, 13] arbitrarily suggested 500 mL of blood loss, as a useful value. In patients with a haematocrit less than 24% and intraoperative blood loss of more than 500 mL, lower 30-day mortality was seen in those who had blood transfusions, compared with those who did not. However, patients with a preoperative haematocrit greater than 30% and loss of more than 500 mL of blood with a subsequent transfusion, according to protocol, had a higher mortality compared to the group without a transfusion. In the intermediate group (haematocrit 24.1–29.9%), either a restrictive or liberal transfusion strategy had no impact on the 30-day mortality. Gregersen et al. studied a group of elderly with frailty syndrome and anaemia and reported that even though a liberal transfusion strategy in the overall group did not raise the 30-day survival rate, the selected group of elderly welfare home residents had a significant extension in 90-day survival rate. No differences were shown between groups in immunological response, infection frequency or quality of life [14]. It seems that when dealing with patients with frailty syndrome, a liberal transfusion strategy has some merit, which is a good basis for further research.

The *method of operative procedure* influences outcomes by affecting the extent of surgical trauma. Many publications in this field emphasise the advantages of laparoscopy with lower blood loss and reduced postoperative pain. This enables early postoperative mobilisation and has a lower risk of postoperative complications such as atelectasis, postoperative bowel obstruction and wound infection. Further complications such as pneumonia, electrolyte or metabolic disturbances, and deep vein thrombosis may be especially troublesome in elderly patients. It is important to emphasise the psychological and social benefits of early mobilisation of older patients, which is necessary for a quick recovery and return to autonomy in everyday life. Laparoscopy limits the extent of inflammation in tissues postoperatively. Indeed, minimally invasive procedures have significantly lower concentrations of proinflammatory cytokines and stress hormones, compared to open

procedures, which produce significantly higher and longer exposure to these compounds [7].

The appropriateness of laparoscopic surgery for patients with severe lung and cardiovascular insufficiency remains debated. Laparoscopic surgery may require a forced and long-lasting body position and prolonged procedure duration and cause an intraperitoneal pressure rise. These are solid arguments for preferring open surgery in this patient group. Therefore, any decision regarding method of procedure should ideally involve multidisciplinary assessment of each individual's potential gains and losses with each approach [15–17].

There is little doubt that the *mode of surgery (emergency or elective)* has a crucial influence on outcome. Emergency surgery in particular is burdened with a higher morbidity and mortality rate. This is due to inability to optimise the patient's general state as well as the advanced pathological processes that are often present because elderly patients may be diagnosed late. Elderly patients may not remember critical elements of their medical history or the medications that they have been prescribed. They may want to wait for family members to be present before making crucial decisions, which in turn further delays commencement of successful treatment. Ideally, elderly patients should be encouraged to undergo elective procedures, ahead of the need for surgery under emergency conditions. Coronary artery bypass surgery, as an ad hoc procedure in the elderly, is associated with mortality rate between 14 and 33%, which falls to 3% in the elective mode. Cholecystectomy has an ad hoc mortality of 5% compared with 0% for elective procedures, while the complication rate was 33% and 3%, respectively. Scheduled laparoscopic gallbladder removal has been shown to be safe in patients with frailty syndrome [18].

Perioperative hypothermia (core temperature below 36 °C) is a frequent problem within the geriatric patient group. Loss of subcutaneous fat tissue and muscle mass together with slower metabolism renders the elderly especially sensitive to surrounding temperature changes with greater difficulty in maintaining normothermia. Low body temperature is a risk factor for postoperative complications such as increased blood loss, coagulation issues, convulsions, impaired wound healing, longer recovery from anaesthesia and cardiovascular complications (including arrhythmia and vasoconstriction caused by increased catecholamine concentrations) [19]. It is also an independent risk factor for postoperative cognitive disorders and delirium [20]. Postoperative convulsions occur infrequently in the geriatric population, but cause a 20–38% rise in metabolic rate. This phenomenon may result in "oxygen deficiency", which may lead to myocardial infarction in the early postoperative period. Moreover, all anaesthetic methods contribute to a decrease in patient core temperature. Some studies suggest the risk is higher with regional anaesthesia. Transfusion of blood products and fluids stored at room temperature, air conditioning in the operating room, a large operating field area and the use of spinal anaesthesia further lower body temperature. Although many guidelines, including the enhanced recovery after surgery protocol, deal with the prevention of hypothermia, it still affects 50–70% of patients [21–23]. Maintaining normothermia reduces cardiovascular complications by 55%. It also reduces the severity of perioperative trauma as determined by proinflammatory cytokines [24]. An exception is made for neurosurgical procedures, where it has been proven that lowering body temperature has a beneficial effect.

Although *anaesthesia* in the twenty-first century is safer than ever before, the percentage of complications associated with anaesthesia alone is around 0.01%. Therefore, the impact of anaesthesia on the patient, which relates to the method chosen, must not be overlooked. The physiological effects of anaesthesia, especially on the elderly, are minimised by technological and pharmacological advances. The aim of anaesthesia is to enable the surgeon to perform efficiently while ensuring the greatest possible comfort and safety for the patient. Existing comorbidities are often the main decisive factor in the geriatric population. The types of surgical anaesthesia used in the elderly do not differ from that used in the general population. All general, spinal and regional anaesthetics are used. However, views on their impact are divided among researchers. Some publications stress that spinal anaesthesia puts less strain on the cardiovascular system and is therefore associated with fewer cardiovascular complications. It is also suggested that maintenance of the patient's own breath leads to less frequent pulmonary complications, reduced blood loss and improved gastrointestinal tract function. Chu et al. and Rodgers et al. screened 128,882 patients over 65 years of age who were undergoing hip surgery and found that those who were generally anaesthetised were more likely to die, be admitted to intensive care units (ICUs), or suffer from stroke or respiratory failure [25, 26]. In patients with chronic obstructive pulmonary disease (COPD), spinal anaesthesia reduces frequency of postoperative pneumonia, unplanned intubations and prolonged intubation (over 48 h) [27].

The use of local anaesthetics under spinal anaesthesia inhibits the endocrine-metabolic response by blocking nociceptive stimulation of the hypothalamus. Extensive epidural blockade with bupivacaine reduces hyperglycaemia, hypercortisolaemia and hypermetabolism resulting in a negative nitrogen balance. Two key factors that inhibit the stressful physiological response are the extent of the blockade and its effectiveness before cutting the skin. The latter is compromised in procedures with immediate indications (waiting time is about 20 min) [28, 29].

On the other hand, subarachnoid anaesthesia affects pain transmission more profoundly than epidural anaesthesia, providing a stronger blockade of both afferent and efferent nerve pathways. As a result, cortisol and glucose responses are

reduced. It might seem that a combination of epidural and subarachnoid blockade, at least in terms of mitigating the cortisol response and perioperative hyperglycaemia, would be ideal for anaesthesia. Dahl et al. used a combination of epidural and subarachnoid blockade including local anaesthetics and opioids with non-steroidal anti-inflammatory drugs (NSAIDs) administered intravenously, and obtained an almost complete inhibition of the cortisol response during colon surgery [30]. However, subarachnoid blockade is an important risk factor for perioperative hypothermia with all its consequences, especially "oxygen deficit". Moreover, the frequently used simultaneous deep sedation (BIS < 50) equates the number of complications of spinal anaesthesia with general anaesthesia. It is also important to recognise that all procedures and manoeuvres performed outside of neurogenic blockade (e.g. tracheal intubation, central vein catheterisation) invariably provoke endocrine and metabolic stress changes.

Balanced analgesia—a combination of general and spinal anaesthesia—seems to be a sought-after "golden mean" of anaesthesia for procedures in general surgery, urology and gynaecology. This anaesthetic technique ideally involves three equally important factors: unconsciousness, analgesia and muscles relaxation. It has been shown to reduce the neuroendocrine response more effectively, by lowering glucose, catecholamine and adrenocorticotrophic hormone concentrations in response to surgical trauma. Yeager et al. demonstrated that lower plasma cortisol concentrations and less frequent infectious complications occur in patients undergoing balanced anaesthesia.

It should also be noted that the immune system's response to local tissue damage does not depend on the type of anaesthesia. As there does not appear to be an advantage of one type of anaesthesia over another, the choice of anaesthetic method is left to the individual assessment of the anaesthetist. Non-medical factors specific to the patient can impact on mental comfort and influence choice of anaesthetic technique. These include anxiety, aversion to being unconscious during the procedure, inability to cooperate and communicate, and inability to lie on one's back for a long time.

We know a little more about the choice of drugs used in general anaesthesia. Approximately 20 years ago, Mitsuhata described the inflammatory response to inhaled anaesthetics compared with propofol. In this study, there were lower concentrations of IL-1.6 and 16 in the sevoflurane group compared to the propofol group while opioid consumption was similar between the two groups. The effect of desflurane on the immune system appears to be much greater than that of sevoflurane, but still less than that of propofol. Isoflurane performed worst of the studied inhaled anaesthetic, with immune response stimulated to a greater degree than with propofol [31, 32].

Some drugs used intraoperatively are associated with an increase in the incidence of postoperative delirium. Pethidine carries the greatest risk (2–7 times higher risk of delirium), followed by long-acting benzodiazepines and barbiturates. Between 15 and 50% of surgical procedures in the elderly are complicated by delirium, which is an independent risk factor for prolonged hospitalisation, incomplete recovery and independence, institutionalisation, dementia and death. However, it is worth noting that the use of regional anaesthesia does not protect against delirium [33, 34].

The aspect of *anaesthetist's experience* as a risk factor for postoperative complications is poorly understood. Cohen et al. analysed 11,000 operations and found no significant correlation between anaesthetist experience or length of anaesthesia and postoperative mortality [35]. However, when analysing complications other than death, Böttger et al. demonstrated a statistically significant correlation between experience and the risk of cardiovascular complications (3-fold increase in risk) and the necessity for prolonged postoperative ventilation (11-fold increase in risk) [36]. Particularly significant was the frequency of postoperative complications when bleeding occurred during the procedure and prolonged procedure duration. There is a lack of research comparing the statistics of complications between countries, especially those which stick firmly to algorithms and those in which individualization of therapy is more frequently used. These comparisons would help assess the extent to which the experience of the anaesthetist influences outcomes.

In terms of *surgeon experience*, several research groups have addressed this issue. Mehta et al. analysed 14,753 emergency general surgery (EGS) procedures and demonstrated that the performance of low-volume (< 25 EGS/year) surgeons was associated with a higher mortality rate but not with occurrence of complications or 30-day readmissions. However, hospital volume was not a protective factor in this matter [37]. Cahill et al. demonstrated that, during the idiopathic correction of teenage scoliosis, an experienced surgeon operated much faster (265 vs 458 min, $p < 0.001$), with lower blood loss (1013 vs 2042 mL, $p < 0.001$) and with better appearance and function evaluation results. Therefore, this study suggested that the results of treatment correlated with surgeon experience [38]. Similar results were confirmed by Meltzer et al., in abdominal aorta aneurysm surgery using endovascular and open methods, and Schmidt et al., in pancreatoduodenectomy [39, 40]. However, several studies have reported that, although less experienced surgeons had longer operation times, the number of complications and the outcomes of oncological treatment were comparable to more experienced colleagues [41, 42]. Interestingly, the number of procedures performed and their repetition are not protective against a natural decrease in performance observed in surgeons after reaching a certain age [43].

In view of the many changes that take place in the body as a result of surgical intervention and the multitude of factors that modify it, surgical teams need tools to support intraoperative assessments. These might involve evaluation of the patient's

condition, prediction of prognosis, and reporting and evaluation of interventions aimed at improving the quality of perioperative care. It is impossible to identify just one key factor of fundamental importance in the intraoperative period. At least a few factors need to be considered. Therefore, evaluation scales have been developed to quantify the individual variables. Complex prediction models such as Acute Physiology and Chronic Health Evaluation (APACHE), Simplified Acute Physiology Score (SAPS) and Physiologic and Operative Severity Score for the Enumeration of Mortality (POSSUM) have proven predictive value in relation to postoperative complications. However, these models have not entered into daily practice in routine evaluation in operating theatres due to the multitude of data needed for analysis and the complexity of the algorithms, which are often impossible to use at bedside. In order for a tool to be valuable, it must be easy to calculate, require minimal resources and have a low cost. In addition, it should be repeatable, validated for individual surgical disciplines and, above all, able to identify patients at risk of serious complications and death, so that these individuals can be monitored closely and treated intensively. In 2007, Gawande et al. developed the Surgical Apgar Score (SAS), which was modelled simply on the ten-point evaluation system for newborns that was introduced just over 50 years prior by Virginia Apgar. Taking into account three parameters available during surgical procedures—estimated blood loss (EBL), lowest mean blood pressure (lowest MAP) and lowest heart rate (lowest HR)—it is possible to identify a group of patients exposed to a statistically higher risk of postoperative complications and death within 30 days of the procedure. Under this scoring system, patients who received 4 or less points were 16 times more likely to suffer from postoperative complications than patients who received 9 or 10 points [44].

The SAS scale was validated in 25 retrospective studies, with 20 confirming the correlation of SAS with severe complications and death within 30 days of the procedure. The predictive properties of SAS were not confirmed in knee alloplasty (Wuerz et al. [45]), hysterectomy with oncological indications (Clark et al. [46]), esophagectomy (Strøyer et al. [47]), neurosurgical procedures within the spine for metastases to bone (Lau et al. [48]), gastrectomy (Miki et al. [49]) and reconstruction operations within the head and neck (Ettinger et al. [50]).

In addition, Regenbogen et al. showed that even if the preoperative evaluation and type of treatment are taken into account, SAS still correlated with the results of surgical treatment ($p < 0.0001$). The frequency of serious complications in the group with a mean SAS score of 7–8 points was equal to the preoperative prognosis (likelihood ratio (LR) 1.05, 95% CI 0.78–1.41), decreased significantly in the group of patients with SAS scores of 9–10 points (LR 0.52, 95% CI 0.35–0.78) and increased significantly for the lowest SAS scores of 5–6 points (LR 1.60, 95% CI 1.12–2.28) and 0–4 points (LR 2.80, 95% CI 1.50–5.21) [51].

It seems that SAS is not suitable for procedures performed under spinal anaesthesia (e.g. knee alloplasty as demonstrated by Wuerz et al. and Thorn et al.), mainly due to hypotension and/or bradycardia occurring after administration of local analgesics to the subarachnoid space [52].

Summary

Surgery and its accompanying procedures are extremely traumatic to the human body, especially for those who are elderly. Their effects are widespread and include the cardiovascular, respiratory, endocrine and immune systems. There are many factors, which together establish the extent of a body's reaction to such a strong stimulus. Some of these are modifiable (e.g. duration of procedure or method used, experience of the surgeon and anaesthetist, blood loss), while some are not (mode of surgery, location). For most procedures, laparoscopy has great advantages even if the duration of surgery is longer. When it comes to blood loss, above 500 mL seems to be an arbitrary value to consider transfusion, which lowers mortality especially if the haematocrit is lower than 24%. The anaesthetist's experience plays a marginal role when following protocols and the surgery is elective. However, the surgeon's experience is an important factor that also predicts the procedure's duration. Preventing hypothermia helps prevent postoperative complications such as increased blood loss, coagulation problems, convulsions, impaired wound healing, longer recovery from anaesthesia and cardiovascular complications. However, while the understanding of the impact of each variable continues to increase, it is still not enough. There is a distinct lack of research concerning the elderly, especially those with frailty syndrome. Much of the existing research does not focus on the elderly in isolation but merely infers detail from the general population. It is important to recognise that the elderly are not simply older adults and extrapolation of the results from younger population studies is likely to have high risk of error. Considering the ageing populations observed on every continent, we see a great need to pursue further research into this matter. This is especially important for elderly patients with frailty syndrome, who are most exposed to perioperative complications, mortality, longer hospital stays and readmissions.

Compliance with Ethical Standards

Conflict of Interest All authors declare that they have no conflicts of interest.

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