A multicentre observational study on management of general anaesthesia in elderly patients at high-risk of postoperative adverse outcomes

Serge Molliex, Passot, Sylvie, Jérôme Morel, Emmanuel Futier, Jean Yves Lefrant, Jean-Michel Constantin, Yannick Le Manach, Bruno Pereira

A multicentre observational study on management of general anaesthesia in elderly patients at high risk of postoperative adverse outcomes

Serge Molliex [a], Sylvie Passot [a], Jerome Morel [a], Emmanuel Futier [b], Jean Yves Lefrant [c], Jean Michel Constantin [b], Yannick Le Manach [d], Bruno Pereira [e], for the Opti-Aged group and Azurea clinical research Network.

[a] Department of Anaesthesiology and Critical Care Medicine, Centre Hospitalier Universitaire (CHU) Saint-Etienne, Université Jean Monnet Saint-Etienne, Saint-Etienne, F-42055 France serge.molliex@chu-st-etienne.fr; sylvie.passot@chu-st-etienne.fr; jerome.morel@chu-st-etienne.fr.

[b] Department of Perioperative Medicine, Centre Hospitalier Universitaire (CHU) Clermont-Ferrand, Université Clermont Auvergne, CNRS, Inserm, Clermont-Ferrand, F-63000 France efutier@chu-clermontferrand.fr; jmconstantin@chu-clermontferrand.fr

[c] Department of Anaesthesiology, Critical Care and Emergency Medicine, Centre Hospitalier Universitaire (CHU) Nîmes, Université de Montpellier-Nîmes, Nîmes, F-30029 France jean.yves.lefrant@chu-nimes.fr

[d] Departments of Anaesthesia and Clinical Epidemiology and Biostatistics, Michael DeGroote School of Medicine, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada. Yannick.Lemanach@phri.ca.

[e] Biostatistic Unit, Direction de la Recherche Clinique (DRCI), Centre Hospitalier Universitaire (CHU) Clermont-Ferrand, Clermont-Ferrand, F-63003 France.
bpereira@chu-clermontferrand.fr .

Note: Contributors of the Opti-aged group are listed in the Appendix.

Correspondence to: S Molliex, Département d'Anesthésie et de Réanimation, CHU Hôpital Nord, 42055 Saint-Etienne Cedex 2, France

serge.molliex@chu-st-etienne.fr

Declaration of interest

S Molliex has received consulting fees, payments and travel funding for lectures from Baxter SA.

E Futier has received consulting fees from Drager Medical and Edwards Lifesciences, and received payments and travel funding for lectures from Drager Medical, GE Healthcare, Fresenius kabi, Baxter, Edwards Healthcare and Fisher & Paykel Healthcare.

JM Constantin reports receiving consulting fees from Baxter, Fresenius Kabi, Dräger, and General Electric Medical Systems, payment for expert testimony from Baxter, Dräger, and Fresenius Kabi, lecture fees from General Electric Medical Systems, Dräger, Fresenius Kabi, Baxter, Hospal, Merck Sharp & Dohme, and LFB Biomedicaments, payment for the development of educational presentations from Dräger, General Electric Medical Systems, Baxter, and Fresenius Kabi, and reimbursement of travel expenses from Bird, Astute Medical, Astellas, Fresenius Kabi, Baxter, and Hospal.

Y. Le Manach is a consultant and has received travel funding for lectures from Edwards SA.

Appendix: Contributors of the Opti-aged Group (n= 84)

The Opti-aged group was formed of investigators issued from 28 French Anaesthesia and Critical Care Departments participating to the Opti-Aged study, a stepped wedge cluster randomized controlled trial to assess the effectiveness of an optimization strategy for general anaesthesia on postoperative morbidity and mortality in elderly patients (ClinicalTrial.gov registration number: NCT02668250).

Centres: contributors

Assistance Publique, Hôpitaux de Marseille, Hôpital de La Timone: N Bruder, C Vaisse.

Assistance Publique, Hôpitaux de Marseille, Hôpital Nord : C Bechis, L Bernard, M Leone, M Poirier, A Vincent.

Assistance Publique, Hôpitaux de Paris, Hôpital Beaujon : N Abdelkrim, C Paugam.

Assistance Publique, Hôpitaux de Paris, Hôpital Bichat : F Lion, P Montravers.

Assistance Publique, Hôpitaux de Paris, Hôpital Pitié-Salpétrière: O Langeron, M Raux.

Assistance Publique, Hôpitaux de Paris, Hôpital Saint Antoine : M Baussier, K Xu

Assistance Publique, Hôpitaux de Paris, Hôpital Saint-Louis et Lariboisière: F Bart, S Dagois, B Plaud, C Rabuel, E Roland.

Centre Hospitalier Universitaire de Bordeaux : M Biais, K Nouette-Gaulain.

Centre Hospitalier Universitaire de Caen : A Cabart, JL Hanouz.

Centre Hospitalier Universitaire de Clermont Ferrand : C Lambert, T Godet, S Thibault.

Centre Hospitalier Universitaire de Dijon : B Bouhemad, E Chambade.

Centre Hospitalier Universitaire de Grenoble : P Bouzat.

Centre Hospitalier Universitaire de Lille, Hôpital Huriez: M Garot, G Lebuffe.

Centre Hospitalier Universitaire de Lille Hôpital Salengro : F Lallemant, C Lemery, B Tavernier.

Centre Hospitalier Universitaire de Montpellier, Hôpital Saint Eloi: A De Jong, S Jaber, D Verzilli.

Centre Hospitalier Universitaire de Nancy : M Delannoy, C Meistelman.

Centre Hospitalier Universitaire de Nice, Hôpital Larchet 2: M Carles, L Tran.

Centre Hospitalier Universitaire de Nîmes : S Bertran, P Cuvillon, J Ripart, S Simon-Pene.

Centre Hospitalier Universitaire de Poitiers : M Boisson, B Debaene.

Centre Hospitalier Universitaire de Rennes : H Beloeil, G Godet.

Centre Hospitalier Universitaire de Strasbourg, Hôpital Central: O Collange, PM Mertes.

Centre Hospitalier Universitaire de Strasbourg, Hôpital de Hautepierre: P Diemunsch, D Joganah, L Oehlkern.

Centre Hospitalier Universitaire de Saint-Etienne : M Baulieu, B Beauchesne, AM Beraud, S Berthier-Berrada, JY Bien, G Dupont, J Gavory, P Lambert, J Lanoiselée, P Zufferey.

Centre Hospitalier Universitaire de Toulouse : F Ferré, C Martin, V Minville, B Planté.

Hospices Civils de Lyon, Centre Hospitalier Lyon Sud: B Baffeleuf, M Ben Abdelkarim, JS David, P Incagnoli, M Khaled, MC Laplace, M Lefevre, V Piriou.

Hospices Civils de Lyon, Hôpital de la Croix Rousse: F Aubrun.

Hospices Civils de Lyon, Hôpital Edouard Herriot: V Cero, C Delsuc, C Faulcon, P Meuret, T Rimmelé, C Truc.

A multicentre observational study on management of general anaesthesia in elderly patients at high risk of postoperative adverse outcomes

Abstract

Introduction: in elderly patients, goal directed haemodynamic therapy (GDHT), depth of anaesthesia monitoring and lung-protective ventilation have been shown to improve postoperative outcomes. The aim of this study was to evaluate current practices concerning strategies of anaesthesia optimisation in patients aged ≥ 75 years.

Patients and methods: a multicentre observational study was performed from February to May 2015 in 23 French academic centres. On 30 consecutive days in each centre, patients ≥ 75 years with at least one major co-morbidity undergoing elective or emergency procedures (femoral-neck fractures surgery, intraperitoneal abdominal surgery or vascular surgery) were included. Patient characteristics and data related to GHDT, management of hypotension, monitoring of temperature and depth of anaesthesia, lung ventilation, point of care haemoglobin testing were collected.

Results: 807 patients were included. Only 2 % of patients [95% CI: 1-3] received GHDT in full accordance with guidelines. Depth of anaesthesia monitoring was largely performed (53%, [95% CI: 50-56]). The multifaceted strategy of lung-protective ventilation combining low tidal volumes (6-8ml/kg), PEEP of 5-8 cm cmH_2O, and repeated recruitment manoeuvres, was performed in only 4 % [95% CI: 3-5] of patients. A centre effect was a major determinant of variation concerning implementation of these strategies.

Discussion: in patients' ≥ 75 years, strategies of anaesthesia optimisation are not in accordance with eligible guidelines. Implementation of these techniques varies independently of factors related to the patient or the type of surgery and may be dependent on the generated constraints.

Keywords: Aged; Anaesthesia management: monitoring; Haemodynamic; Ventilation

Introduction

Elderly patients constitute an increasingly large proportion of high surgical risk patients. Their management in major surgery is associated with significant postoperative morbidity and mortality. Postoperative deaths in patients over 70 years represent 80 % of the overall postoperative mortality in the UK [1]. In high-risk surgical patients, several studies have demonstrated that goal directed haemodynamic therapy (GHDT) significantly reduced postoperative mortality and morbidity [2,3], and that a combination of excessive depth of anaesthesia measured by bispectral index, hypotension and low anaesthesia requirement resulted in increased mortality [4,5] Guidance from NICE [6,7] have mandated the use of cardiac output monitoring and depth of anaesthesia monitoring in patients at higher risks of adverse outcomes in an attempt to improve their outcomes. The use of these two monitoring is thus recommended in aged patients alongside a conventional monitoring including pulse oximetry, capnography, ECG and blood pressure and core temperature monitoring [8,9]. Lung-protective ventilation strategy was also associated with improved postoperative outcomes in patients at risk of pulmonary complications that include elderly patients [10, 11]. Combining these strategies optimising anaesthesia could reduce the build-up of oxygen debt and act synergistically to decrease postoperative morbidity. Additional monitoring and related strategies of anaesthesia optimisation are not used as frequently as they should be in the elderly patient's population [12]. The present study involving 23 French academic centres was aimed at assessing the current practice concerning monitoring and intraoperative strategies of general anaesthesia optimisation in patient's ≥ 75 years at high risk of adverse outcomes, and determining factors associated with their use.

Patients and Methods

This prospective study was approved by the Comité de Protection des Personnes Sud-Est 6 of the Clermont-Ferrand University Hospital (ref 2015/CE11) and was performed from February to May 2015 in 23 academic centres regrouping 28 anaesthesia departments (Appendix : Opti-aged group contributors). Due to the observational nature of the study, informed consent was waived according to the French law, but all patients were informed about the study and had the opportunity to refuse to participate. On 30 consecutive days in each department, all the patients aged ≥ 75 years undergoing elective or emergency femoral-neck fractures surgery, intraperitoneal abdominal surgery (excluding cholecystectomy, abdominal wall surgery and minor surgery), or vascular surgery (excluding arterio-venous fistula and venous surgery) were included.

The surgical procedures were selected following analysis of the 2010 French Hospital Discharge database (PMSI) which contains medical procedures for all patients admitted to public and private hospitals in 2010, identified by their code according to medical classification for clinical procedures and discharge diagnoses encoded in the International Classification of Diseases, 10th revision (ICD-10 codes). These procedures were chosen because they were associated with a 24.0 % [95% CI: 23.7-24.4] incidence of a composite criteria combining 30-day major postoperative complications (acute kidney injury, acute myocardial infarction, heart failure, stroke, severe sepsis, septic shock, acute respiratory failure requiring non-invasive ventilation or intubation, delirium) and mortality in patients aged ≥ 75 years having at least one comorbidity among the following: ischaemic coronary disease, cardiac arrhythmia, congestive heart failure, peripheral vascular disease, dementia, stroke, chronic obstructive pulmonary disease (COPD), chronic respiratory failure, chronic alcohol abuse, active cancer, diabetes, chronic renal failure.

All participants were included from induction of anaesthesia to the end of surgery and received general anaesthesia. The study had an online application for collecting and managing data on patients recruited. The physicians had to fill an electronic case report form (eCRF) with the following patient variables: age (≥75 or ≥ 80 years), ASA score (I, II, III, IV, V), comorbidities (ischemic coronary disease, cardiac arrhythmia, congestive heart failure, peripheral vascular disease, dementia, stroke, chronic obstructive pulmonary disease, chronic respiratory failure, chronic alcohol abuse, active cancer, diabetes), type (femoral-neck fracture surgery, intraperitoneal abdominal surgery, vascular surgery) and nature (elective, emergency) of the surgery. Data collected are shown in Table 1. Data were collected as yes or no responses except for temperature at the end of surgery, value of blood pressure defining hypotension, tidal volume and PEEP level where quantitative parameters were required.

For a rate of adhesion to the recommendations expected between 20% and 50%, inclusion of 800 patients allows to evaluate the rate of adhesion (α = 5% 1-β =80%) with a margin of error of 3,5%.

Statistical analysis was performed using Stata 13 software (StataCorp LP, College Station, TX, US). The tests were two-sided, with a type I error set at α = 0.05. Subject’s characteristics were presented as median [range] for continuous data (assumption of normality was assessed using the Shapiro–Wilk test) and as the number of patients and associated percentages with 95%CI for categorical parameters. Comparisons between the independent groups were performed using the chi-squared or Fisher’s exact tests for categorical variables, and using Student t-test or Mann-Whitney test for quantitative parameters (normality, assumption of homoscedasticity studied using Fisher-Snedecor test). As proposed by some statisticians, we chose to report all the individual p-values without applying any mathematical correction for distinct tests comparing groups. Specific attention was given to the magnitude of improvement and to clinical relevance. Multivariate analysis was performed using generalized linear mixed model (with logit link function for dichotomous dependent outcome). The covariates, considered as fixed effects, were retained according to univariate results and to their clinical relevance. The centre effect has been considered as random-effect in order to take into account between and within centre variability. Indeed, observations from the same centre (cluster) could be usually considered more similar to each other than observations from different centres. The intra-class correlation coefficient (ICC), ratio of the between-centre variance to the total variance, could be seen as the proportion of the total variance of dependent outcome that is accounted for by the clustering centre effect. It could also be interpreted as the correlation among observations within the same centre. Results were expressed by intra-class correlation coefficient (ICC) and using forest-plots presenting risk-ratios and 95% confidence intervals. As less than 5% of data were missing for each variable of interest, handling of missing data was not applied.

Results

During the study period from February 1, 2015 and through May 31, 2015 a total of 1013 patients were screened for eligibility in the study and 807 were ultimately included. One hundred and forty six patients did not meet comorbidity inclusion criteria, 37 and 23 patients, those of age and type of surgery respectively. Patients' characteristics are shown in Table 2. Patients were mainly high-risk patients (71% ASA ≥ III), having elective surgery (59%) equally distributed among the 3 types of surgery. Cardiovascular comorbidity was the most frequently observed (62% of patients).

A protocol-based treatment of hypotension was used in 63 % [95%CI: 60-66] of the patients (Fig 1 [A, B]). IOH was predominantly defined as a decrease of mean blood pressure (51%, [95% CI: 48-54]), below a certain absolute threshold (72 %, [95% CI: 69-75]). The median of this threshold (range) was 70 (50-90) mmHg. When a decrease in blood pressure relative to the patients' baseline mean blood pressure was reported, the median drop (range) was 30 (10-30) %. When IOH definition was based on systolic blood pressure, the median threshold (range) and the median drop (range) were respectively of 100 (80-150) mmHg and 20 (10-30) %. The vasopressor mainly used to treat hypotension was ephedrine in 43% [95% CI: 40-47] of cases. Vascular surgery (RR [95%CI]: 4.82 [2.40-9.66] $p < 0.001$) and intraperitoneal abdominal surgery (RR [95%CI]: 2.39 [1.35-4.23] $p= 0.003$) were the 2 determinants associated with the existence of a protocol-based treatment of hypotension within the same centre (Fig 2).

Cardiac output or stroke volume (SV) monitoring was used in 10 % [95% CI: 8-12] of patients (Fig [1 A, C]). The research of SV plateau value by initial fluid challenge was performed in 25% [95% CI: 15-34] of monitored patients. Moreover, one in two patients did not benefit of intraoperative SV optimisation with fluid. Finally, fourteen patients received goal directed therapy (GDT) fully respecting the NICE and the French Society of Anaesthesia and Intensive Care Medicine (SFAR) published algorithms. Intraperitoneal abdominal surgery (RR [95%CI]:

3.07 [1.39-6.79] p= 0.006) was associated with stroke volume monitoring within the same centre (Fig 2).

EEG depth of anaesthesia monitoring was performed in 53% of patients [95% CI: 50-56]. (Fig 1 [A, D]). In the majority of cases (85% [95% CI: 83-89]) a 40-60 index objective was observed. Maintenance of anaesthesia was started when BIS index or SE entropy index was higher than a threshold value in only 25 % [95% CI: 21-29] of monitored patients. The suppression ratio (RS) or burst suppression ratio (BSR) was monitored in 23% [95% CI: 19-27] of cases. Intraperitoneal abdominal surgery (RR [95%CI]: 1.80 [1.09-2.97] p=0.021), emergency procedures (RR [95%CI]: 1.65 [1.05-2.60] p=0.028) were associated with EEG depth of anaesthesia monitoring within the same centre (Fig 2).

Tidal volume was mainly chosen on the basis of predicted ideal body weight (74% [95% CI: 71-77]), the median tidal volume (range) was 7(5-10) ml/kg (Fig 1 [A, E]). When tidal volume used actual body weight, the median tidal volume was also 7(5-10) ml/kg. Thirty-six patients (4%) underwent recruitment manoeuvres after induction of anaesthesia and every 30 min during surgery. PEEP was used in most cases (94% [95% CI: 92-96]). The median (range) PEEP was 5 (2-12] cmH_2O. PEEP was < 5 cmH_2O in 175 patients (22%). Multifaceted strategy of protective-lung ventilation that combined low tidal volumes (6-8ml/kg of ideal predicted body weight), a PEEP of 5-8 cm cmH_2O and recruitment manoeuvre repeated every 30 min after tracheal intubation (9) was performed in only 33 patients (4% [95% CI: 3-5]). No factor related to the patients or the type of surgery was associated with the completion of a recruitment manoeuver within the same centre (Fig 2).

Temperature was monitored in 70% [95% CI: 67-73] of patients. Median temperature (range) was 36.2° [32.6°- 38.3°] at the end of surgery. Intraperitoneal abdominal surgery (RR

[95%CI]: 3.11 [1.62-5.96] p=0.001) and cardiovascular comorbidities (RR [95%CI]: 0.35 [0.16-0.76] p=0.008) were the two factors influencing the use of temperature monitoring within the same centre (Fig 2).

A point of care haemoglobin testing was performed in 347 patients (43%) representing 51%, 45% and 31% of patients undergoing femoral neck fractures, intraperitoneal and vascular surgery respectively. Ninety-eight patients received intraoperative red blood cells transfusion (12%) [femoral neck surgery: n= 32 (12%); intraperitoneal abdominal surgery: n= 37 (12%); vascular surgery : n= 29 (12%)]. The thresholds of haemoglobin considered for transfusion were between 70g/l and 100g/l (Table 3). In 46 patients over 98 (47%) receiving RBC transfusion in the absence of ischemic coronary disease, the threshold of transfusion used was higher than recommended by the NICE and the French Haute Autorité de Santé (HAS) guidelines [13,14].

Regardless of the monitoring and the related optimisation strategies of anaesthesia, the high values of ICC coefficient between 0.24 and 0.45 demonstrated that the centre effect was a major determinant of variation concerning implementation of these techniques and strategies in elderly patients (Fig 3).

Discussion

The main findings of this study are that in elderly patients with high risk of major postoperative complications, monitoring and related strategies of general anaesthesia optimisation are not in accordance with eligible guidelines and evidence, and that the implementation of these techniques varies greatly from one centre to another, independently of factors related to the patient co-morbidities or the type of surgery but appears related to the constraint generated.

Haemodynamic monitoring and management in elderly patients had the low compliance rate with guidelines. Only 1.7 % of patients received GDHT in full accordance with the algorithm recommended by the SFAR or ESA guidelines [15, 16]. Results can be explained by several reasons [17]. Physicians can consider that monitoring cardiac output remains too invasive in many cases, despite available technologies with minimal invasiveness that may facilitate its clinical implementation [18]. They may prefer the use of dynamic predictors of fluid responsiveness as surrogate of cardiac output. Recent evidence also suggests that GDT is not bringing the added benefit to the care of surgical high-risk patients that was previously described [19-21], specifically in patients undergoing hip fracture surgery [22]. The rate of adhesion to the recommendations may also be related to the lack of strong level of evidence in elderly patients. The validation of SV-based algorithms in this population where the high incidence of diastolic dysfunction means the ability to increase SV is limited [22], needs to be addressed. Goal directed haemodynamic therapy also requires frequent assessment of fluid responsiveness, and may increase provider workload in the busy operating room environment limiting its implementation in clinical practice. The lack of education on how to use the devices may add an additional barrier to their use and the cost of these devices may be a burden for the implementation of Goal Directed Therapy concepts. Finally, a limited access to monitors may also contribute to our results as suggested in a survey amongst North American and European anaesthesiologists [18]. In addition, more than a third of patients did not benefit from a protocol-based treatment of hypotension. However, this did not prejudge that hypotension was not rapidly treated by the anaesthetist during surgery. Our results confirm that there is no accepted single definition for IOH due to the absence of a solid evidence-based threshold value at which to treat low blood pressures [23]. It is nevertheless surprising that the existence of a protocol-based treatment of IOH was only related to the type of surgery and not to the patient's cardiovascular comorbidities. Management targeting an individualised blood pressure in patients who were at increased postoperative risk reduced the risk of postoperative organ dysfunction in a recently published study [24].

Depth of anaesthesia was monitored in 53% of patients although the causal relationship between low processed EEG values and poor outcomes is lacking [25-27]. The relatively frequent use of depth of anaesthesia monitoring in elderly patients may be related to that the fact that increased age did not change the BIS index associated with clinical endpoints for sedation [28], while the influence of aging on pharmacology is an important factor in determining anaesthetic requirements. During general anaesthesia, a suppression ratio (RS or BSR) >0 is mainly produced by unnecessarily deep anaesthesia excepting cases of severe hypothermia and rare cerebral ischemic insults [29]. It is thus an intriguing finding of our study that this ratio was only monitored in 23% of patients where BIS or entropy was used. In accordance with NICE and NHS recommendations, high risk surgery represented by the emergency procedures was found to be an independent factor associated with depth of anaesthesia monitoring.

A strategy of low tidal volume ventilation was used in a majority of patients with a 5 cm H_2O median PEEP value. Twenty-two percent of patients received a low level of PEEP (< 5 cm H_2O). The optimum level of positive PEEP for prophylactic lung-protective ventilation is unknown [30] but the use of low levels of PEEP may lead to atelectasis by promoting repeated opening and closing of small airways [31] and could be harmful in some patients. In a study of 29 343 patients who underwent general anaesthesia with mechanical ventilation, the use of low tidal volume (6-8 ml Kg^{-1} IBW) and minimum levels of PEEP was associated with an increased risk of 30-day mortality [32]. Moreover, alveolar recruitment manoeuvres are mandatory to fully open collapsed alveoli, while PEEP is needed to prevent further collapse. In our study, only 4% of patients underwent adherence to the multifaceted strategy of protective-lung ventilation associated with improved clinical outcomes in intermediate- and high-risk patients [10, 11]. The recruitment manoeuvres that represent the binding part of this strategy were rarely performed and repeated, whereas the setting a low tidal volume with a peep was a more common practice. This can also be related to the lack of standardisation in the way the recruitment manoeuvres are performed [11]. Questions also remains concerning the effective recruitment pressures and the minimal duration required for these inspiratory pressures to recruit the collapsed lungs of most patients under general anaesthesia, as well as regarding the safety of these manoeuvres [11].

Our results are in agreement with previously published surveys concerning haemodynamic management and monitoring suggesting a gap between evidence about the benefits of perioperative haemodynamic optimisation and the clinical practice [18, 33-34]. According to our results, in a recent large and retrospective cohort, the use of protective intraoperative mechanical ventilation was driven by the individual preference/practice of the anaesthesia provider, rather than patient and/or procedural characteristics [35]. The mean probability of administering protective ventilation was 53.8% in the latter study but protective ventilation definition included a median positive end-expiratory pressure of 5 cm H_2O or more, tidal volume of <10 mL/kg of predicted body weight and plateau pressure of <30 cm H_2O but no recruitment manoeuvres [35]. Concerning depth of anaesthesia monitoring, in retrospectively collected intraoperative data on 55,210 surgical cases at a tertiary care hospital, factors associated with BIS® use included: increased age, greater ASA physical status, extremes of Body Mass Index (BMI), use of intravenous anaesthetics, use of long-acting paralytic agent, use of an endotracheal tube, emergency surgery, increasing length of case, an certain type of surgery [36]. In our study, age and ASA physical status were not factors associated with the use of depth of anaesthesia monitoring because only aged patients ≥ 75 years with at least one comorbidity (ASA ≥ 2) were included.

The present study has several limitations. First, the study was declarative and exposed to a non-response bias and to the Hawthorne effect. The latter may have led to an overestimation of the use of additional monitoring and related strategies for optimizing anaesthesia. The lack of consensus about application of certain guidelines to the elderly or to the type of surgical procedures included in our study may also be discussed. Our study was not designed to evaluate postoperative patient outcomes and the effect of each recommendation could affect patient outcomes in different ways. Our cross sectional evaluation was mainly focused on 4 approaches (Blood pressure management, GDHT, depth of anaesthesia monitoring and protective ventilation) whose common pathophysiology is to prevent or reduce the build-up of intraoperative oxygen debt. However, the benefit of this multimodal monitoring on post-operative morbidity and mortality has not been reported. This study was performed exclusively in University hospitals where many high-risk surgeries are achieved in elderly, and monitoring devices are supposed to be more frequently available. Thus, the generalizability of our results can be reasonably considered.

Conclusion

These results demonstrate a considerable gap between clinical practice and guidelines concerning anaesthetic optimisation in elderly patients at increased postoperative risk. In addition, clinical practice is heavily influenced by local factors that may not be justified by the recently published evidence. We postulate that implementation of a multimodal strategy of anaesthesia optimisation is mainly dependent of the constraints generated. Closed-loop automation of anaesthetics and fluid administration, as well as the automation of alveolar recruitment by the ventilator may represent an interesting approach in this context. The benefit of such multimodal optimisation strategy has to be addressed in elderly patients.

References

[1] National Confidential Enquiring into Patient Outcome and Death. Knowing the risk. A review of the peri-operative care of surgical patients, http://www.ncepod.org.uk/2011report2/downloads/POC_fullreport.pdf ; 2011 [accessed 18 December 2017].

[2] Gurgel ST, do Nascimento P, Jr. Maintaining tissue perfusion in high-risk surgical patients: a systematic review of randomized clinical trials. Anesth Analg 2011;112:1384-91.

[3] Hamilton MA, Cecconi M, Rhodes A. A systematic review and meta-analysis on the use of preemptive hemodynamic intervention to improve postoperative outcomes in moderate and high-risk surgical patients. Anesth Analg 2011; 112:1392-402.

[4] Sessler DI, Sigl JC, Kelley SD, Chamoun NG, Manberg PJ, Saager L, et al. Hospital stay and mortality are increased in patients having a "triple low" of low blood pressure, low bispectral index, and low minimum alveolar concentration of volatile anaesthesia. Anesthesiology 2012;116:1195-203.

[5] Willingham MD, Karren E, Shanks AM, O'Connor MF, Jacobsohn E, Kheterpal S, et al. Concurrence of Intraoperative Hypotension, Low Minimum Alveolar Concentration, and Low Bispectral Index Is Associated with Postoperative Death. Anesthesiology 2015;123:775-85.

[6] National Institute of Health and Care Excellence. MTG 3. CardioQ-ODM oesophageal Doppler monitor, https://www.nice.org.uk/guidance/mtg3 ; 2011 [accessed 18 December 2017].

[7] National Institute for Health and Clinical Excellence. NICE diagnostics guidance. Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M, https://www.nice.org.uk/dg6; 2012 [accessed 18 December 2017].

[8] Griffiths R, Alper J, Beckingsale A, Goldhill D, Heyburn G, Holloway J, et al. Management of proximal femoral fractures 2011: Association of Anaesthetists of Great Britain and Ireland. Anaesthesia 2012;67:85-98.

[9] Griffiths R, Beech F, Brown A, Dhesi J, Foo I, Goodall J, et al. Peri-operative care of the elderly 2014: Association of Anaesthetists of Great Britain and Ireland. Anaesthesia 2014; 69 (Suppl 1), 81-98.

[10] Futier E, Constantin JM, Paugam-Burtz C, Pascal J, Eurin M, Neuschwander A, et al. A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. N Engl J Med 2013;369:428-37.

[11] Güldner A, Kiss T, Neto AS, Hemmes SNT, Canet J, Spieth PM et al. Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications. A comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. Anesthesiology 2015; 123:692-713.

[12] National Confidential Enquiring into Patient Outcome and Death. An Age Old Problem. A review of the care received by elderly patients undergoing surgery, http://www.ncepod.org.uk/2010report3/downloads/EESE_fullReport.pdf; 2010 [accessed 18 December 2017].

[13] National Institute for Health and Clinical Excellence. NICE Guidelines. Blood Transfusion, http://www.nice.org.uk/guidance/ng24; 2015 [accessed 18 December 2017].

[14] Haute Autorité de Santé. Recommandations de Bonnes Pratiques. Transfusion de globules rouges homologues: produits, indications, alternatives, https://www.has-

sante.fr/portail/upload/docs/application/pdf/2015-02/transfusion_de_globules_rouges_homologues_-_produits_indications_alternatives_-_recommandations.pdf ; 2014 [accessed 18 December 2017].

[15] Vallet B, Blanloeil Y, Cholley B, Orliaguet G, Pierre S, Tavernier B. [Guidelines for perioperative haemodynamic optimization. Societe française d'anesthésie et de réanimation]. Ann Fr Anesth Reanim 2013;32:454-62.

[16] European Society of Anaesthesiology. Perioperative Goal-Directed Therapy Protocol Summary, http://html.esahq.org/patientsafetykit/resources/downloads/05_Checklists/Various_Checklists/Perioperative_Goal_Directed_Therapy_Protocols.pdf; 2013 [accessed 18 December 2017].

[17] Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. JAMA 1999; 282: 1458-65.

[18] Cannesson M, Pestel G, Ricks C, Hoeft A, Perel A. Hemodynamic monitoring and management in patients undergoing high risk surgery: a survey among North American and European anesthesiologists. Crit Care 2011;15:R197.

[19] Arulkumaran N, Corredor C, Hamilton MA, Ball J, Grounds RM, Rhodes A, et al. Cardiac complications associated with goal-directed therapy in high-risk surgical patients: a meta-analysis. Br J Anaesth 2014;112:648-59.

[20] Challand C, Struthers R, Sneyd JR, Erasmus PD, Mellor N, Hosie KB, et al. Randomized controlled trial of intraoperative goal-directed fluid therapy in aerobically fit and unfit patients having major colorectal surgery. Br J Anaesth 2012;108:53-62.

[21] Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, et al. Effect of a perioperative, cardiac output-guided hemodynamic therapy algorithm on outcomes following major gastrointestinal surgery: a randomized clinical trial and systematic review. JAMA 2014;311:2181-90.

[22] Moppett IK, Rowlands M, Mannings A, Moran CG, Wiles MD. LiDCO-based fluid management in patients undergoing hip fracture surgery under spinal anaesthesia: a randomized trial and systematic review. Br J Anaesth 2015;114:444-59.

[23] Bijker JB, van Klei WA, Vergouwe Y, Eleveld DJ, van Wolfswinkel L, Moons KG, et al. Intraoperative hypotension and 1-year mortality after noncardiac surgery. Anesthesiology 2009;111:1217-26.

[24] Futier E, Lefrant JY, Guinot PG, Godet T, Lorne E, Cuvillon P, et al. Effect of individualized vs standard blood pressure aanagement strategies on postoperative organ dysfunction among high-risk patients undergoing major surgery. A randomized clinical trial.

JAMA 2017; 318: 1346-57.

[25] Short TG, Leslie K, Campbell D, Chan MT, Corcoran T, O'Loughlin E, et al. A pilot study for a prospective, randomized, double-blind trial of the influence of anesthetic depth on long-term outcome. Anesth Analg 2014;118:981-6.

[26] Kertai MD, Pal N, Palanca BJ, Lin N, Searleman SA, Zhang L, et al. Association of perioperative risk factors and cumulative duration of low bispectral index with intermediate-term mortality after cardiac surgery in the B-Unaware Trial. Anesthesiology 2010;112:1116-27.

[27] Kertai MD, Palanca BJ, Pal N, Burnside BA, Zhang L, Sadiq F, et al. Bispectral index monitoring, duration of bispectral index below 45, patient risk factors, and intermediate-term mortality after noncardiac surgery in the B-Unaware Trial. Anesthesiology 2011;114:545-56.

[28] Katoh T, Bito H, Sato S. Influence of age on hypnotic requirement, bispectral index, and 95% spectral edge frequency associated with sedation induced by sevoflurane. Anesthesiology 2000;92:55-61.

[29] Purdon PL, Sampson A, Pavone KJ, Brown EN. Clinical Electroencephalography for Anesthesiologists: Part I: Background and Basic Signatures. Anesthesiology 2015;123:937-60.

[30] Futier E, Jaber S. Lung-protective ventilation in abdominal surgery. Curr Opin Crit Care 2014;20:426-30.

[31] Bendixen HH, Hedley-Whyte J, Laver MB. Impaired Oxygenation in Surgical Patients during General Anaesthesia with Controlled Ventilation. A Concept of Atelectasis. N Engl J Med 1963;269:991-6.

[32] Levin MA, McCormick PJ, Lin HM, Hosseinian L, Fischer GW. Low intraoperative tidal volume ventilation with minimal PEEP is associated with increased mortality. Br J Anaesth 2014;113:97-108.

[33] Suehiro K, Tanaka K, Mukai A, Joosten A, Desebbe O, Alexander B, et al. Hemodynamic monitoring and management in high-risk surgery: a survey among Japanese anesthesiologists. J Anesth 2016; 30:526-29.

[34] Kim SH, Kim MJ, Lee JH, Cho SH, Chae WS, Cannesson M. Current practice in hemodynamic monitoring and management in high-risk surgery patients: a national survey of Korean anesthesiologists. Korean J Anesthesiol 2013; July 65: 19-32.

[35] Ladha KS, Bateman BT, Houle TT, De Jong MAC, Vidal Melo MF, Huybrechts KF, et al. Variability in the use of protective mechanical ventilation during general anesthesia. Anesth Analg 2018;126: 503-12.

[36] Gelfand ME, Gabriel RA, Gimlich R, Beutler SS, Urman RD. Practice patterns in the intraoperative use of bispectral index monitoring. J Clin Monit Comput 2017; 31:281-89.

Table 1: Parameters of optimisation strategy of general anaesthesia, and related guidelines or references.

Parameters		Guidelines or references (reference)

Blood pressure monitoring
- protocol-based treatment for intraoperative hypotension
- type of threshold value defining hypotension
    - systolic arterial pressure
    - mean arterial pressure
- definition of threshold value
    - absolute
    - relative
- threshold value
- type of vasopressor used to treat hypotension
    - ephedrine
    - phenylephrine
    -noradrenaline
		(8,9)

Monitoring of stroke volume (SV)
- type of monitor
    - esophageal Doppler
    - pulse contour analysis
    -other
- research of SV plateau value by initial fluid challenge
- intraoperative fluid challenge when SV reduction > 10%
		(6, 8, 15, 16)

EEG depth of anaesthesia monitoring
- type of monitor
    - BIS®
    - Entropy®
    - other
- 40-60 target objective
- threshold value to start maintenance of anaesthesia
- suppression ratio (SR) or burst suppression ratio (BSR) monitoring
		(7,8,9)

Lung protective ventilation - tidal volume (ml/kg) - tidal volume based on ideal predicted body weight - recruitment manoeuvres immediately applied after intubation - intraoperative recruitment manoeuvres - inspired oxygen fraction (FiO_2) < 50% - PEEP level (cmH_2O)		(10-11, 30)
Haemoglobin (Hb) testing and transfusion **-** point of care haemoglobin testing - blood transfusion - red blood cells (RBC) transfusion threshold		(13, 14)
Temperature monitoring **-**temperature at the end of surgery		(8,9)

Table 2: Patients characteristics. Data are expressed as number (percentage of patients included in the study).

	Number of patients (%)
Age	
75-79	254 (31)
≥80	553 (69)
ASA score	
II	208 (29)
III	456 (63)
IV	57 (8)
V	1 (0)
Type of surgery	
Femoral neck fracture	260 (32)
Intraperitoneal abdominal	301 (38)
Vascular	241 (30)
Nature of surgery	
Elective	443 (59)
Emergency	306 (41)
Comorbidities	
Ischemic coronary disease	203 (25)
Cardiac arrhythmia	273 (34)
Congestive heart failure	136 (17)
Peripheral vascular disease	204 (25)
Dementia	162 (20)
Stroke	145 (18)
Chronic obstructive pulmonary disease	100 (12)
Chronic respiratory failure	51 (6)
Chronic alcohol abuse	23 (3)
Active cancer	181 (22)
Diabetes	184 (23)

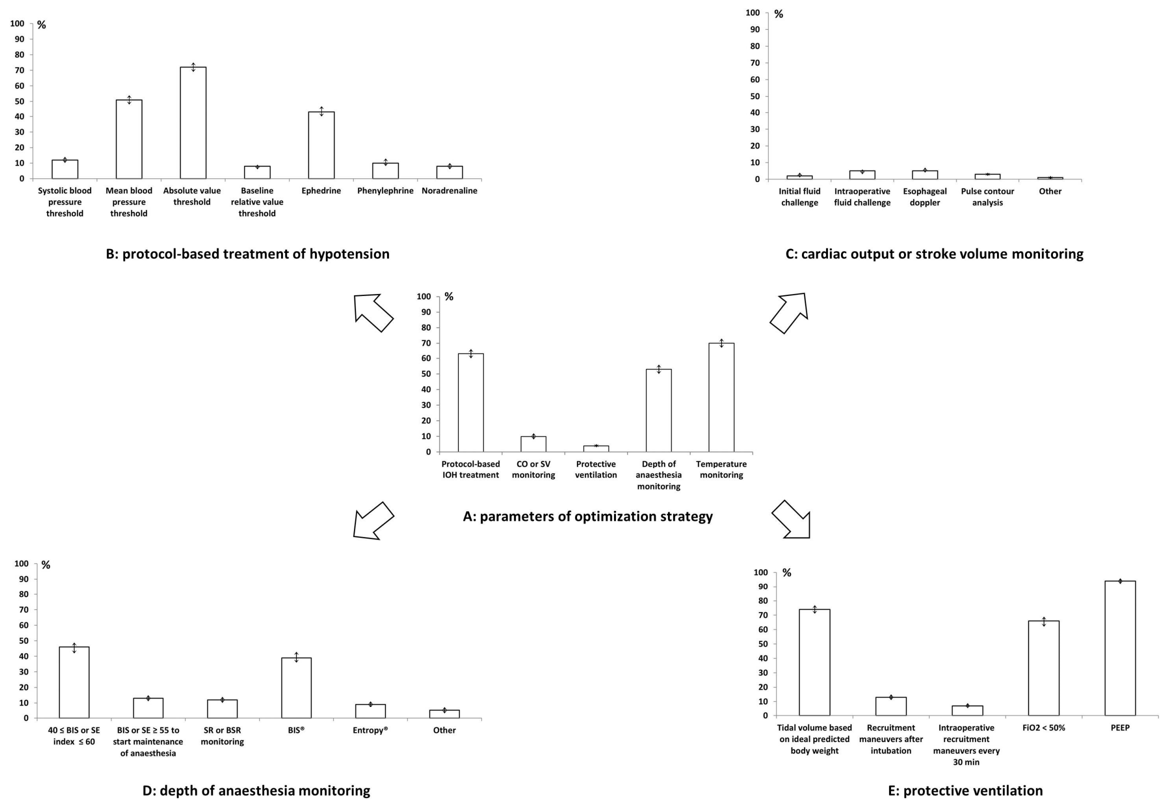
Table 3: Thresholds of haemoglobin for red blood cells (RBC) transfusion and absence of cardiovascular comorbidities. Data are expressed as number [percentage of patients receiving RBC].

Threshold of haemoglobin (g/l)	**Patients transfused (n) [% of patients receiving RBC]**	**No ischemic coronary disease comorbidity (n)**	**No cardiovascular comorbidities (n)**
10	39 [40]	23	10
9	31 [32]	15	7
8	22 [22]	8	5
7	6 [6]	0	0

Figure 1: Monitoring and related optimisation strategies of anaesthesia. Data are expressed as percentage of patients included in the study. A: different parameters of optimisation strategies; B: protocol-based treatment of hypotension; C: cardiac output (CO) or stroke volume (SV) monitoring; D: Depth of anaesthesia monitoring, SE: state entropy, SR: suppression ratio, BSR: burst suppression ratio; E: protective ventilation. The 95% confidence interval of the percentage is plotted by arrows.

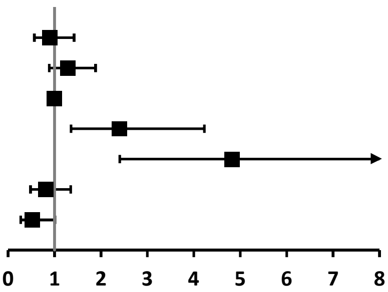
Figure 2: Factors associated with monitoring and intraoperative strategies of optimisation of general anaesthesia.

Figure 3: Intra-class correlation coefficient (ICC), ratio of the between-centre variance to the total variance for each parameter of optimisation strategies. It could be seen as the proportion of the total variance of dependent outcome that is accounted for by the clustering centre effect.


B: protocol-based treatment of hypotension
Systolic blood pressure threshold
Mean blood pressure threshold
Absolute value threshold
Baseline relative value threshold
Ephedrine
Phenylephrine
Noradrenaline
C: cardiac output or stroke volume monitoring
Initial fluid challenge
Intraoperative fluid challenge
Esophageal doppler
Pulse contour analysis
Other
A: parameters of optimization strategy
Protocol-based IOH treatment
CO or SV monitoring
Protective ventilation
Depth of anaesthesia monitoring
Temperature monitoring
D: depth of anaesthesia monitoring
40 ≤ BIS or SE index ≤ 60
BIS or SE ≥ 55 to start maintenance of anaesthesia
SR or BSR monitoring
BIS®
Entropy®
Other
E: protective ventilation
Tidal volume based on ideal predicted body weight
Recruitment maneuvers after intubation
Intraoperative recruitment maneuvers every 30 min
FiO2 < 50%
PEEP

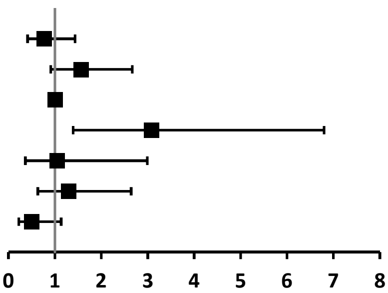
Protocol-based treatment of hypotension.

	Risk ratio	95% CI	p-value
Age	0.897	[0.566 ; 1.422]	0.644
ASA physical status	1.292	[0.885 ; 1.886]	0.184
HIP fracture surgery	1.000	[0.990 ; 1.010]	1.000
Intraperitoneal abdominal surgery	2.398	[1.359 ; 4.231]	0.003
Vascular surgery	4.823	[2.407 ; 9.667]	<0.001
Emergency vs. elective surgery	0.807	[0.483 ; 1.349]	0.413
Cardiovascular comorbidities	0.523	[0.271 ; 1.010]	0.054



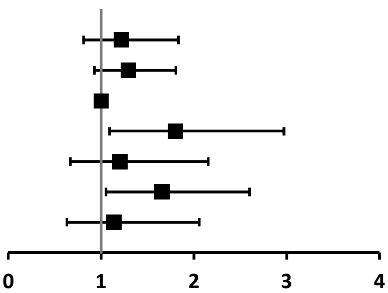
Stroke volume monitoring

	Risk ratio	95% CI	p-value
Age	0.771	[0.413 ; 1.438]	0.413
ASA physical status	1.561	[0.913 ; 2.669]	0.104
HIP fracture surgery	1.000	[0.990 ; 1.010]	1.000
Intraperitoneal abdominal surgery	3.075	[1.391 ; 6.798]	0.006
Vascular surgery	1.044	[0.365 ; 2.991]	0.936
Emergency vs. elective surgery	1.293	[0.632 ; 2.645]	0.482
Cardiovascular comorbidities	0.504	[0.223 ; 1.139]	0.100



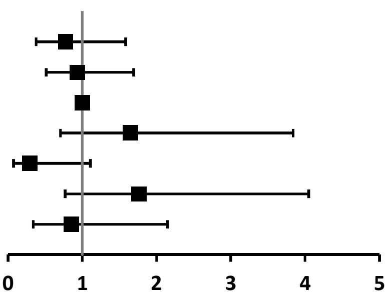
EEG depth of anaesthesia monitoring.

	Risk ratio	95% CI	p-value
Age	1.221	[0.813 ; 1.834]	0.336
ASA physical status	1.294	[0.928 ; 1.804]	0.129
HIP fracture surgery	1.000	[0.990 ; 1.010]	1.000
Intraperitoneal abdominal surgery	1.802	[1.092 ; 2.973]	0.021
Vascular surgery	1.201	[0.669 ; 2.155]	0.539
Emergency vs. elective surgery	1.656	[1.055 ; 2.600]	0.028
Cardiovascular comorbidities	1.139	[0.630 ; 2.059]	0.666



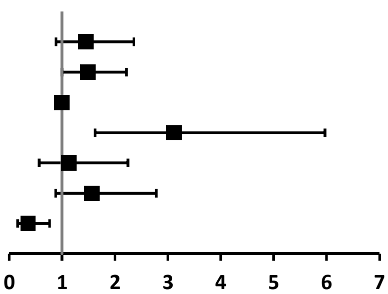
Intraoperative recruitment maneuvers.

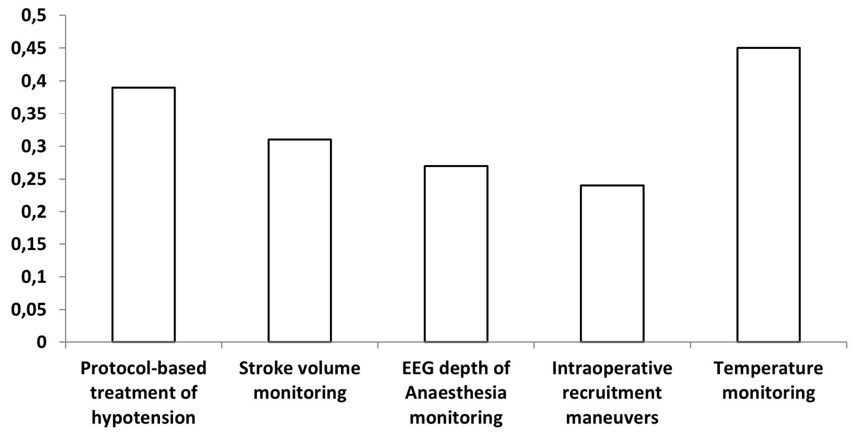
	Risk ratio	95% CI	p-value
Age	0.775	[0.379 ; 1.582]	0.483
ASA physical status	0.931	[0.513 ; 1.692]	0.816
HIP fracture surgery	1.000	[0.990 ; 1.010]	1.000
Intraperitoneal abdominal surgery	1.643	[0.704 ; 3.837]	0.251
Vascular surgery	0.287	[0.074 ; 1.108]	0.070
Emergency vs. elective surgery	1.762	[0.767 ; 4.048]	0.182
Cardiovascular comorbidities	0.853	[0.339 ; 2.147]	0.736



Temperature monitoring.

	Risk ratio	95% CI	p-value
Age	1.447	[0.887 ; 2.360]	0.139
ASA physical status	1.488	[0.998 ; 2.219]	0.051
HIP fracture surgery	1.000	[0.990 ; 1.010]	1.000
Intraperitoneal abdominal surgery	3.113	[1.624 ; 5.969]	0.001
Vascular surgery	1.128	[0.566 ; 2.248]	0.732
Emergency vs. elective surgery	1.563	[0.878 ; 2.783]	0.129
Cardiovascular comorbidities	0.353	[0.162 ; 0.766]	0.008




0,5
0,45
0,4
0,35
0,3
0,25
0,2
0,15
0,1
0,05
0
Protocol-based treatment of hypotension
Stroke volume monitoring
EEG depth of Anaesthesia monitoring
Intraoperative recruitment maneuvers
Temperature monitoring