

ORIGINAL RESEARCH ARTICLE

Intraoperative hypotension when using hypotension prediction index software during major noncardiac surgery: a European multicentre prospective observational registry (EU HYPROTECT)

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Abstract

Background: Intraoperative hypotension is associated with organ injury. Current intraoperative arterial pressure management is mainly reactive. Predictive haemodynamic monitoring may help clinicians reduce intraoperative hypotension. The Acumen™ Hypotension Prediction Index software (HPI-software) (Edwards Lifesciences, Irvine, CA, USA) was developed to predict hypotension. We built up the European multicentre, prospective, observational EU HYPROTECT Registry to describe the incidence, duration, and severity of intraoperative hypotension when using HPI-software monitoring in patients having noncardiac surgery.

Methods: We enrolled 749 patients having elective major noncardiac surgery in 12 medical centres in five European countries. Patients were monitored using the HPI-software. We quantified hypotension using the time-weighted average MAP <65 mm Hg (primary endpoint), the proportion of patients with at least one ≥1 min episode of a MAP <65 mm Hg, the number of ≥1 min episodes of a MAP <65 mm Hg, and duration patients spent below a MAP of 65 mm Hg.

Received: 18 February 2023; Accepted: 28 March 2023

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Results: We included 702 patients in the final analysis. The median time-weighted average MAP <65 mm Hg was 0.03 (0.00–0.20) mm Hg. In addition, 285 patients (41%) had no ≥ 1 min episode of a MAP <65 mm Hg; 417 patients (59%) had at least one. The median number of ≥ 1 min episodes of a MAP <65 mm Hg was 1 (0–3). Patients spent a median of 2 (0–9) min below a MAP of 65 mm Hg.

Conclusions: The median time-weighted average MAP <65 mm Hg was very low in patients in this registry. This suggests that using HPI-software monitoring may help reduce the duration and severity of intraoperative hypotension in patients having noncardiac surgery.

Keywords: artificial intelligence; blood pressure; haemodynamic instability; haemodynamic monitoring; machine learning; postoperative complications

Arterial pressure is a major determinant of organ perfusion.¹ Arterial hypotension is a key feature of haemodynamic instability.² In patients having surgery, intraoperative hypotension is common^{3–5} and associated with organ injury^{6–10} and death.^{6,11–13} It thus seems advisable to avoid intraoperative hypotension.^{14,15}

However, avoiding intraoperative hypotension during major surgery is challenging.¹⁶ It requires close arterial pressure monitoring^{17,18} and rapid treatment of low arterial pressures according to the presumed aetiology.^{1,19} Current haemodynamic management is still mainly reactive, with hypotension being treated only after it has occurred.

Predictive haemodynamic monitoring may be a promising approach to help clinicians reduce the incidence and severity of intraoperative hypotension. The Acumen™ Hypotension Prediction Index software (HPI-software) (Edwards Lifesciences, Irvine, CA, USA) was developed using machine learning to predict arterial hypotension defined as a MAP of less than 65 mm Hg for at least 1 min.²⁰ By analysing arterial pressure waveform features, it quantifies the likelihood that a patient will develop hypotension on a unitless scale between 0 and 100.²⁰ HPI values over 85 trigger acoustic and visual alarms and a pop-up window providing the possibility to display additional haemodynamic variables that might guide clinicians in treating the cause of hypotension.

There are only sparse data on the effect of using HPI-software monitoring on intraoperative hypotension in patients having elective major noncardiac surgery. We thus aimed to quantify the amount of intraoperative hypotension when using HPI-software monitoring. We therefore built up the European multicentre, prospective, observational EU HYPROTECT Registry to describe the incidence, duration, and severity of intraoperative hypotension when using HPI-software monitoring in patients having noncardiac surgery.²¹

Methods

Study design and objective

We registered the EU HYPROTECT Registry at [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT04972266) on July 22, 2021, and we published the details of the study protocol and methods.²¹ In short, EU HYPROTECT was a European multicentre, prospective, observational registry in patients having elective major noncardiac surgery in 12 medical centres in five European countries (France, Germany, Italy, Spain, and United Kingdom). Ethics committee approvals were obtained for each site. Patients gave written informed consent to participate in the registry (unless the need for informed consent was waived by the local ethics committee). The overarching objective of the registry

was to quantify intraoperative hypotension when using HPI-software monitoring in patients having elective major noncardiac surgery.

Study protocol

Patients in the registry were monitored using the Acumen™ IQ sensor (Edwards Lifesciences) and the HemoSphere monitoring platform (Edwards Lifesciences), which calculates and continuously displays HPI and haemodynamic variables, including arterial pressure. Because using HPI-software monitoring requires training and education, the registry was performed in medical centres that routinely use HPI-software monitoring with the Acumen™ IQ sensor and the HemoSphere monitoring platform. There was no specific treatment protocol for patients included in this registry; patients were treated according to each centre's clinical routine. HPI-software monitoring and data recording were started with the beginning of surgery and stopped when surgery ended.

Patients

We planned to include at least 700 patients in the registry. We included consenting adults (≥ 18 yr) who were scheduled for elective major noncardiac surgery under general anaesthesia that was expected to last at least 120 min and in whom intra-arterial pressure and HPI-software monitoring were planned for clinical management. We did not include patients having emergency surgery, nephrectomy, and liver or kidney transplantation; patients with atrial fibrillation or sepsis (according to The Third International Consensus Definitions for Sepsis and Septic Shock); patients with ASA physical status classification 5 or 6; patients who were not able to understand the nature, significance, and scope of the investigation; pregnant women; patients without signed informed consent; and patients participating in interventional trials.

Endpoints

We aimed to describe the incidence, duration, and severity of intraoperative hypotension when using HPI-software monitoring in patients having elective major noncardiac surgery. The primary endpoint was the time-weighted average MAP <65 mm Hg. The time-weighted average MAP <65 mm Hg (unit: mm Hg) is the area under a MAP of 65 mm Hg (unit: mm Hg $\times$ minutes) divided by the total monitoring time (i.e. the total duration of surgery; unit: minutes).^{22,23} We also report the time-weighted average MAP <60 and <55 mm Hg; the area under a MAP of 65, 60, and 55 mm Hg; the proportion of patients with at least one ≥ 1 min episode of a MAP <65, <60, and

<55 mm Hg; number of ≥ 1 min episodes of a MAP <65, <60, and <55 mm Hg; absolute duration and relative duration (% of surgical time) patients spent below a MAP of 65, 60, and 55 mm Hg; and the absolute maximum decrease lasting ≥ 1 min below a MAP of 65, 60, and 55 mm Hg. We further calculated the time-weighted average MAP >100 mm Hg and the absolute and relative duration (% of surgical time) patients spent above a MAP of 100 mm Hg.

On an exploratory basis, we describe the incidence of (i) acute myocardial injury within three days after surgery, (ii) acute kidney injury within three and seven days after surgery, (iii) death within 30 days after surgery, (iv) hospital readmission within 30 days after surgery, and (v) a composite outcome of non-fatal cardiac arrest and death within 30 days after surgery. For this purpose, we followed patients for 30 days after surgery (via a telephone call if the patient left the hospital earlier than 30 days after surgery).

Acute myocardial injury was defined according to the definition of 'myocardial injury and infarction associated with noncardiac procedures' provided in the Fourth Universal Definition of Myocardial Infarction (2018)²⁴ as an increase in high-sensitivity troponin T or I concentrations above the sex-specific 99th percentile upper reference limit within the first three postoperative days with (i) a $\geq 50\%$ increase when the initial troponin T or I concentration was below the sex-specific 99th percentile upper reference limit, or (ii) a $\geq 20\%$ increase when the initial troponin T or I concentration was above the sex-specific 99th percentile upper reference limit. We considered high-sensitivity troponin T or I values (whichever were used in each centre) when measured per routine care before surgery and on postoperative Days 1, 2, or 3 (Supplementary Table 1).

Acute kidney injury was defined based on the Kidney Disease: Improving Global Outcomes Clinical Practice Guideline for Acute Kidney Injury^{25,26} as (i) an increase in serum creatinine concentration of ≥ 0.3 mg dl⁻¹ within any 48 h period within the first seven postoperative days, (ii) an increase in serum creatinine of $\geq 50\%$ from baseline within the first seven postoperative days, or (iii) the need for renal replacement therapy within the first seven postoperative days. We considered serum creatinine values when measured per routine care before surgery (baseline) and on postoperative Days 1–7 (Supplementary Table 2). We only considered the serum creatinine and renal replacement criteria (i.e. excluding the urine output criterion) in accordance with current recommendations^{25,26} because urine output is usually not reliably recorded after surgery.

Non-fatal cardiac arrest was defined as successful resuscitation from ventricular fibrillation, ventricular tachycardia, asystole, or pulseless electrical activity requiring cardiopulmonary resuscitation, pharmacological therapy, or cardiac defibrillation.

Further, we report the ICU length of stay and the hospital length of stay.

Statistical analysis

We performed descriptive analyses to quantify intraoperative hypotension, patient characteristics, and perioperative data. Continuous variables are presented as median (25th percentile–75th percentile), and categorical variables are presented as absolute number (percentage). All statistical analyses were performed using IBM SPSS Statistics version 24

(IBM, Armonk, NY, USA) or R Core Team (<https://www.R-project.org/>).

The sample size was estimated based on previously published data. A randomised trial reported a median time-weighted average MAP <65 mm Hg of 0.44 (0.23–0.72) mm Hg without and 0.10 (0.01–0.43) mm Hg with HPI-software monitoring.²³ Considering the wide inter-quartile range of the time-weighted average MAP <65 mm Hg, we planned to include at least 700 patients.

Results

Between September 2021 and May 2022, we enrolled 749 patients in the registry. We excluded 47 patients because of inclusion or exclusion criteria violation ($n=33$), technical problems with HPI-software monitoring or recording ($n=10$), or lack of study personnel to initiate HPI-software monitoring ($n=4$). We thus finally included 702 patients in the analysis (Table 1). The patients' median age was 64 (55–73) yr; 340 patients (48%) were female.

The patients had surgery for a median of 209 (153–290) min. All patients had surgery under general anaesthesia, either as total intravenous anaesthesia (234 patients [33%]) or balanced anaesthesia (467 patients [67%]) (Table 2); 332 patients (47%) additionally had neuraxial or regional anaesthesia. During

Table 1 Baseline and clinical characteristics ($n=702$). Categorical data are presented as absolute number (percentage) and continuous data as median (25th percentile–75th percentile). Percentages may not sum up to 100% because of rounding. n , absolute number.

Variable	Value
Characteristics	
Age (yr)	64 (55–73)
BMI (kg m ⁻²)	26.2 (23.4–29.4)
Sex, n	
Male	362 (52)
Female	340 (48)
ASA physical status, n	
1	27 (4)
2	374 (53)
3	296 (42)
4	5 (1)
Baseline risk factors, n	
Chronic arterial hypertension	363 (52)
Antihypertensive medication	351 (50)
Diabetes mellitus	104 (15)
Oral hypoglycaemic agent	82 (12)
Chronic heart failure	17 (2)
Coronary artery disease	52 (7)
Cerebrovascular disease	25 (4)
Chronic obstructive pulmonary disease	71 (10)
Chronic kidney injury	42 (6)
Type of surgery, n	
General surgery	250 (36)
Gynaecological surgery	105 (15)
Neurosurgery	76 (11)
Orthopaedic surgery	21 (3)
Spine surgery	33 (5)
Thoracic surgery	35 (5)
Urological surgery	98 (14)
Vascular surgery	76 (11)
Other	8 (1)

Table 2 Intraoperative clinical characteristics (n=702). Categorical data are presented as absolute number (percentage) and continuous data as median (25th percentile–75th percentile). n, absolute number.

Variable	Value
Type of anaesthesia, n	
Balanced anaesthesia	467 (67)
Total intravenous anaesthesia	234 (33)
Thoracic epidural	140 (20)
Lumbar epidural	33 (5)
Spinal anaesthesia	97 (14)
Peripheral regional anaesthesia	62 (9)
Vasoactive drug administration	
Cafedrine/theodrenaline, n=126 (ml)	2.0 (1.0–2.5)
Epinephrine, n=13 (mg)	9 (1.2–12.8)
Ephedrine, n=134 (mg)	18 (9–24)
Metaraminol, n=50 (mg)	8.1 (3.9–13.3)
Norepinephrine, n=502 (mg)	1.3 (0.6–2.6)
Dobutamine, n=69 (mg)	36.5 (15.3–50.7)
Phenylephrine, n=96 (mg)	0.3 (0.2–0.8)
Fluid management	
Colloid fluid (ml)	600 (500–1000)
Crystalloid fluid (ml)	2400 (1500–3600)
Red blood cell transfusion, n	106 (15)
Fresh frozen plasma transfusion, n	52 (7)
Platelet transfusion, n	9 (1)
Cell saver autotransfusion, n	12 (2)
Estimated blood loss (ml)	250 (100–500)
Estimated urine output (ml)	550 (300–1048)
Postoperative destination, n	
PACU	400 (57)
ICU	302 (43)

surgery, the patients were given a median total volume of crystalloid and colloid fluids of 2500 (1500–3537) ml. Vaso-pressors or inotropes were administered in 639 patients (91%): 502 (79%) patients were given norepinephrine, 134 (21%) ephedrine, 126 (20%) cafedrine/theodrenaline, 96 (15%) phenylephrine, and 69 (11%) dobutamine.

The median time-weighted average MAP <65 mm Hg was 0.03 (0.00–0.20) mm Hg. There were 285 patients (41%) who had no ≥ 1 min episode of a MAP <65 mm Hg; 417 patients (59%) had at least one (Table 3). The median number of ≥ 1 min episodes of a MAP <65 mm Hg was 1 (0–3). Patients spent a median of 2.0 (0.0–9.1) min or 1 (0–5)% of surgical time below a MAP of 65 mm Hg. The median absolute maximum decrease lasting ≥ 1 min below a MAP of 65 mm Hg was 7 (3–12) mm Hg. The median time-weighted average MAP >100 mm Hg was 0.25 (0.02–0.08) mm Hg, and patients spent a median of 7.8 (1.0–23.3) min above a MAP of 100 mm Hg.

There were 21 patients (3%) who had acute myocardial injury within three days of surgery, and four of them fulfilled the definition of myocardial infarction. There were 62 patients (9%) who had an acute kidney injury within three days of surgery and 79 (11%) within seven days. Fifty-five patients (8%) were re-admitted to hospital within 30 days of surgery. Patients stayed in the ICU for 1 (1–2) day and in the hospital for 6 (4–9) days after surgery. The composite outcome of non-fatal cardiac arrest or death within 30 days after surgery occurred in 12 patients (2%); 11 patients (2%) died within 30 days after surgery.

Table 3 Arterial pressure and clinical outcomes (n=702). Categorical data are presented as absolute number (percentage) and continuous data as median (25th percentile–75th percentile). n, absolute number.

Variable	Value
Time-weighted average MAP values (mm Hg)	
<65 mm Hg	0.03 (0.0–0.2)
<60 mm Hg	0.0 (0.0–0.05)
<55 mm Hg	0.0 (0.0–0.0)
Area under MAP values (mm Hg $\times$ min)	
<65 mm Hg	6.1 (0.0–42.3)
<60 mm Hg	0.01 (0.0–8.8)
<55 mm Hg	0.0 (0.0–0.8)
Proportion of patients with at least one ≥ 1 min episode below MAP thresholds (%)	
<65 mm Hg	59.4
<60 mm Hg	37.9
<50 mm Hg	9.8
Number of ≥ 1 min episodes below MAP thresholds, n	
<65 mm Hg	1 (0–3)
<60 mm Hg	0 (0–1)
<55 mm Hg	0 (0–0)
Absolute duration below MAP thresholds (min)	
<65 mm Hg	2.0 (0.0–9.1)
<60 mm Hg	0.0 (0.0–2.0)
<55 mm Hg	0.0 (0.0–0.0)
Relative duration (% of surgical time) below MAP thresholds (%)	
<65 mm Hg	1.0 (0.0–4.5)
<60 mm Hg	0.0 (0.0–1.0)
<55 mm Hg	0.0 (0.0–0.0)
Absolute maximum decrease lasting ≥ 1 min below MAP thresholds (mm Hg)	
<65 mm Hg	7 (3–12)
<60 mm Hg	6 (3–10)
<55 mm Hg	5 (2–8)
Time-weighted average MAP >100 mm Hg (mm Hg)	0.25 (0.02–0.08)
Absolute duration above a MAP >100 mm Hg (min)	7.8 (1.0–23.3)
Relative duration (% of surgical time) above a MAP >100 mm Hg (%)	3.9 (0.5–11.6)
Postoperative complications, n	
Acute myocardial injury	21 (3)
Acute kidney injury within three days after surgery	62 (9)
Acute kidney injury within seven days after surgery	79 (11)
Non-fatal cardiac arrest	2 (0.3)
Death	11 (2)
Hospital re-admission	55 (8)

Discussion

The median time-weighted average MAP <65 mm Hg was very low in patients in this registry. This suggests that using HPI-software monitoring may help reduce the duration and severity of intraoperative hypotension in patients having noncardiac surgery. The median time-weighted average MAP <65 mm Hg was 0.03 mm Hg. About 40% of the patients had no ≥ 1 min episode of MAP <65 mm Hg. Patients had a MAP <65 mm Hg for a median of 2 min or 1% of surgical time.

Both the duration and severity of intraoperative hypotension are associated with postoperative complications.²⁷ We thus primarily quantified intraoperative hypotension as time-weighted average MAP <65 mm Hg because it reflects both hypotension duration and severity. Patients in this registry had a median time-weighted average MAP <65 of 0.03 mm Hg, which is substantially lower than those reported previously in patients having major noncardiac surgery (Fig 1).^{23,28–30}

In patients randomly allocated to receive routine care in three trials on HPI-software-guided intraoperative arterial pressure management, the median time-weighted average MAP <65 mm Hg were 0.44,²³ 0.14,²⁸ and 0.50 mm Hg.³⁰ Interestingly, even in patients randomised to HPI-software-guided intraoperative arterial pressure management, the time-weighted average MAP <65 mm Hg was substantially higher than in patients included in this registry: 0.10,²³ 0.14,²⁸ and 0.16 mm Hg³⁰ vs 0.03 mm Hg in this registry. Similarly, in a retrospective observational study, including 100 patients having noncardiac surgery, the median time-weighted average MAP <65 mm Hg was 0.27 mm Hg when patients were treated based on pulse wave analysis data without HPI-software monitoring and 0.10 mm Hg when HPI-software monitoring was used as well.²⁹

There are presumably different reasons why there was little intraoperative hypotension in patients in this registry. First, the HPI-software may predict hypotension several minutes before a hypotensive event occurs.^{20,31} The very purpose of the HPI-software monitoring thus is to allow the treatment of impending hypotension before it occurs. Second, using HPI-software monitoring requires training and education. We only recruited patients in medical centres where HPI-software monitoring is used per clinical routine. Most clinicians taking care of registry patients thus had experience with using HPI-software monitoring. Third, when considering the additional haemodynamic data provided on the secondary screen, HPI-

software monitoring helps in treating or preventing intraoperative hypotension specifically and causally. The secondary screen provides advanced haemodynamic variables and enables identifying and specifically treating the most likely cause of (impending) hypotension. Common causes of intraoperative hypotension include vasodilation, hypovolaemia, and impaired myocardial contractility,^{19,32} all of which require specific treatment. Clinicians treating registry patients seemingly treated intraoperative hypotension causally by using different vasopressors and inotropes and different types of fluids. For example, around 45% of all patients received two different types of vasoactive drugs, with norepinephrine, ephedrine, and cafedrine/theodrenaline being the ones most frequently used.

Intraoperative hypotension is a modifiable risk factor for postoperative organ injury.^{14,15} Although the threshold for harm in individual patients remains unclear, intraoperative hypotension at some level likely causes organ injury. We thus also explored perfusion-related outcomes, including acute myocardial and kidney injury and other patient-centred outcomes. Only 3% of patients had acute myocardial injury within three days after surgery. A low burden of intraoperative hypotension may have contributed to the low incidence of acute myocardial injury. However, we did not systematically measure postoperative troponin concentrations.³³ Instead, we considered troponin values when measured for clinical indications. It has repeatedly been shown that acute myocardial injury is missed without systematic postoperative troponin screening.^{34,35} About 9% of the patients had acute kidney injury within three days after surgery. However, we also did not systematically measure serum creatinine after surgery but only considered serum creatinine values when measured for clinical indications. But, in contrast to troponin, serum creatinine is routinely measured after surgery in most participating medical centres. Postoperative mortality within 30 days after

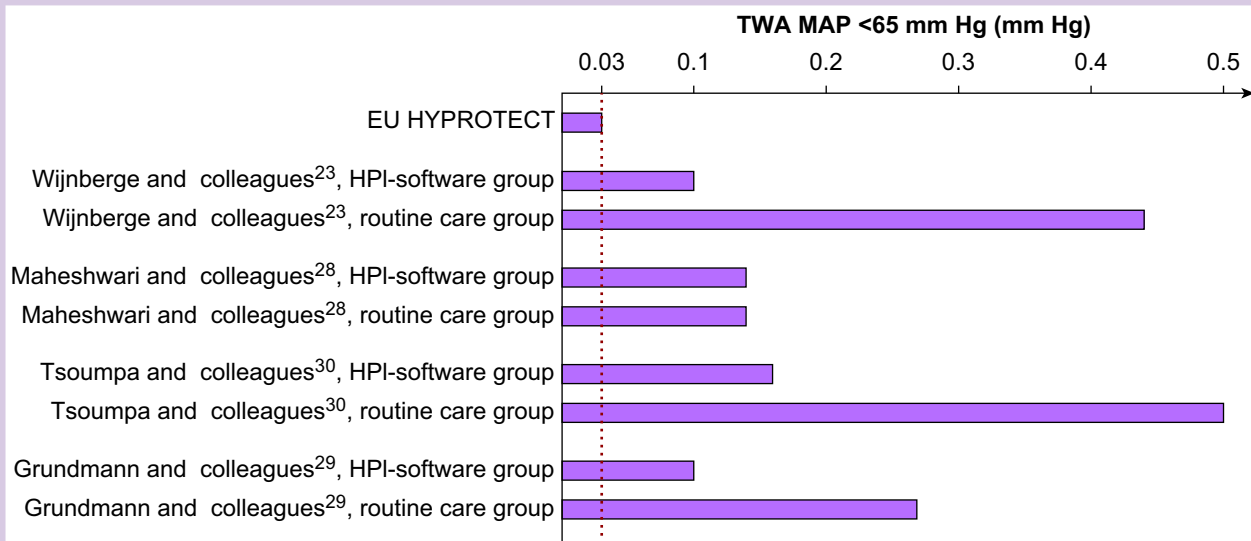


Fig 1. Bar chart illustrating the time-weighted average MAP (TWA MAP) <65 mm Hg in patients of this registry and of previously published studies on Hypotension Prediction Index software (HPI-software) monitoring.^{23,28–30}

surgery was observed in 2% of patients, which is consistent with postoperative mortality in Europe³⁶ and the USA.³⁷ Large randomised trials are necessary to test the hypothesis that HPI-software-guided, compared with routine, arterial pressure management improves patient-centred outcomes in patients having surgery.

A strength of this multicentre European registry is that it reflects hypotension exposure and clinical outcomes in a wide range of patients having noncardiac surgery monitored with HPI-software. Therefore, the results of this registry can inform the design and sample-size calculation of robust randomised trials investigating whether HPI-software-guided arterial pressure management reduces intraoperative hypotension and eventually perfusion-related patient-centred outcomes. Such trials are needed because previous trials on HPI-software-guided arterial pressure management were small, only powered to investigate hypotension reduction, and showed conflicting results.^{28,38} The main limitation of this registry is that it does not allow us to directly compare intraoperative arterial pressures between patients with vs without HPI-software-guided haemodynamic management. We thus naturally cannot infer that using HPI-software monitoring was the only reason that there was little hypotension. Only randomised trials can answer the question whether there is a causal effect of HPI-software-guided hypotension reduction on patient outcome. However, comparing the median time-weighted average MAP <65 mm Hg observed in our registry patients with those from previous studies and trials suggests that the use of HPI-software monitoring contributed to hypotension reduction.

In summary, the median time-weighted average MAP <65 mm Hg was very low in patients in this European multicentre, prospective, observational registry. This suggests that using HPI-software monitoring may help reduce the duration and severity of intraoperative hypotension in patients having noncardiac surgery. However, randomised trials are needed to investigate whether HPI-software-guided haemodynamic management improves patient-centred outcomes by reducing hypotension.

Authors' contributions

Study conception/design: KK, MIMG, MS, DG-L, EG, PB, BS
 Study measurements: KK, EC, IL, GD, LF, MS, AAA, UHF, CDG, SJD, AD, JR-M, DG-L, BV, EG, EN, BS
 Data analysis/interpretation: all authors
 Statistical analysis: PB
 Drafting of paper: KK, PB, BS
 Critical revision of paper for important intellectual content: MIMG, EC, IL, GD, LF, MS, AAA, UHF, CDG, SJD, AD, JR-M, DG-L, BV, EG, EN.
 Final approval of the version to be published: all authors
 All authors are accountable for all aspects of the work.

Funding

Edwards Lifesciences.

Declarations of interest

KK, LF, MS, UHF, CDG, JR-M, and DG-L are consultants for and have received honoraria for giving lectures from Edwards Lifesciences (Irvine, CA, USA). KK is a consultant for Vygon (Aachen, Germany). MIMG has been an employee of Edwards

Lifesciences at the onset of the registry. EC has received honoraria for giving lectures from Edwards Lifesciences and MSD (Puteaux, France). MS has received research funding for investigator-initiated trials from Edwards Lifesciences, is a consultant for and has received honoraria for giving lectures from AMOMED (Vienna, Austria), and has received honoraria for giving lectures from Orion Pharma (Hamburg, Germany). AAA and BV have received honoraria for giving lectures from Edwards Lifesciences. UHF has received honoraria for giving lectures from CSL Behring (King of Prussia, PA, USA). SJD is a consultant for and has received honoraria for giving lectures and restricted and unrestricted research grants from Edwards Lifesciences. BV is a consultant for Ratiopharm GmbH (Ulm, Germany). EG is a consultant for Edwards Lifesciences and has received consultant fees from Baxter (Deerfield, IL, USA) and research grants from Radiometer (Krefeld, Germany) and Philips (Böblingen, Germany). EN is a consultant for and received honoraria from Edwards Lifesciences, Masimo (Neuchâtel, Switzerland), and MSD. PB is a consultant for Edwards Lifesciences, and his institution IPPMed received research funding for the organisation of this project. BS is a consultant for and has received institutional restricted research grants and honoraria for giving lectures from Edwards Lifesciences, Baxter, GE Healthcare (Chicago, IL, USA), and Pulsion Medical Systems SE (Feldkirchen, Germany); is a consultant for and has received honoraria for giving lectures from Philips Medizin Systeme Böblingen GmbH (Böblingen, Germany); has received institutional restricted research grants and honoraria for giving lectures from CNSystems Medizintechnik GmbH (Graz, Austria); is a consultant for Maquet Critical Care (Solna, Sweden); has received honoraria for giving lectures from Getinge (Gothenburg, Sweden); is a consultant for and has received honoraria for giving lectures from Vygon; is a consultant for and has received institutional restricted research grants from Retia Medical LLC (Valhalla, NY, USA); has received institutional restricted research grants from Osypka Medical (Berlin, Germany); and was a consultant for and has received institutional restricted research grants from Tensys Medical, Inc. (San Diego, CA, USA). IL, GD, and AD declared to have no potential conflicts of interest.

Acknowledgements

The authors acknowledge the contribution of the staff at Edwards Lifesciences, especially Edward Hembrow, Tim van den Boom, Anne Halfmann, Pierre Sibilleau, Barbara Plaschaert, Volker Haag, Giulia Torricella, and Alessia Longo. The authors further appreciate the excellent project management secured by Daniel Greinert, Marie Zielinski, and Claudia Lüske at the Institute for Pharmacology and Preventive Medicine (Cloppenburg, Germany). Edwards Lifesciences had an active role in the design of the study and acts as the legal sponsor.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bjao.2023.100140>.

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Handling Editor: Phil Hopkins