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Individualized Cardiac Index–Guided Hemodynamic Therapy in High-Risk Patients Undergoing Elective Major Abdominal Surgery
The PELICAN Randomized Clinical Trial

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IMPORTANCE It remains unclear if intraoperative hemodynamic therapy should be guided by cardiac index.

OBJECTIVE To evaluate whether individualized cardiac index–guided hemodynamic therapy vs routine hemodynamic therapy improves outcomes in high-risk patients undergoing elective major abdominal surgery.

DESIGN, SETTING, AND PARTICIPANTS This multicenter, single-blind, superiority randomized clinical trial enrolled high-risk patients undergoing elective major abdominal surgery between October 8, 2023, and October 25, 2025, at 12 university medical centers in Austria, the Czech Republic, Denmark, Germany, and Spain. The date of last follow-up was January 15, 2026.

INTERVENTIONS Patients were randomized to individualized cardiac index–guided hemodynamic therapy targeting the patient's preoperative resting cardiac index vs routine hemodynamic therapy (with blinded cardiac index monitoring).

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death within the first 7 postoperative days. Secondary outcomes included the individual components of the primary outcome within the first 7 postoperative days.

RESULTS Of the 1128 patients enrolled, 1111 were randomized and 1095 were included in the primary analysis (median age, 67 years [IQR, 59-74 years]; 49.4% were female). The primary outcome occurred in 243 of 549 patients (44.3%) in the individualized cardiac index–guided hemodynamic therapy group vs 256 of 546 patients (46.9%) in the routine hemodynamic therapy group (relative risk, 0.94 [95.1% CI, 0.83-1.08]; *P* = .38). There were no between-group differences for the incidence of the individual components of the primary outcome within the first 7 postoperative days.

CONCLUSIONS AND RELEVANCE Among high-risk patients undergoing elective major abdominal surgery, individualized cardiac index–guided hemodynamic therapy targeting the patient's preoperative resting cardiac index did not reduce the incidence of a composite outcome of acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death within the first 7 postoperative days compared with routine hemodynamic therapy.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT05648279

Visual Abstract
Research Summary
Supplemental content

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In patients undergoing major noncardiac surgery, intraoperative hemodynamic therapy is intended to preserve adequate tissue perfusion and oxygenation to prevent organ injury.[1-3] Tissue perfusion and oxygenation are determined by both arterial blood pressure and cardiac index (ie, cardiac output indexed to body surface area).[4]

Blood pressure must be monitored in every patient undergoing surgery,[2,5,6] and current guidelines recommend keeping intraoperative mean arterial pressure above 60 to 65 mm Hg.[2,7,8] In contrast, cardiac index is not routinely monitored,[9,10] and it remains unclear if intraoperative hemodynamic therapy should be guided by cardiac index. In addition, existing guidelines do not specify what constitutes adequate cardiac index during surgery.[7,8] In 2 previous multicenter trials, maximizing intraoperative cardiac index by giving fluids and inotropes did not improve patient-centered outcomes.[11,12] In contrast, we considered the theory that intraoperative cardiac index should be individualized and maintained at each patient's preoperative resting value.[13]

Therefore, we conducted a multicenter trial to test the hypothesis that individualized cardiac index-guided hemodynamic therapy targeting the patient's preoperative resting cardiac index reduces the incidence of a composite outcome of acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death within the first 7 postoperative days compared with routine hemodynamic therapy in high-risk patients undergoing elective major abdominal surgery.

Key Points

Question Does individualized cardiac index–guided hemodynamic therapy targeting preoperative resting cardiac index improve outcomes in high-risk patients undergoing elective major abdominal surgery?

Findings In this randomized clinical trial including 1128 patients, there was no significant between-group difference for the incidence of the composite primary outcome (acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death within 7 postoperative days) among patients in the individualized cardiac index–guided hemodynamic therapy group (44.3%) vs the routine hemodynamic therapy group (46.9%).

Meaning These findings do not support individualized cardiac index–guided hemodynamic therapy targeting the preoperative resting cardiac index in high-risk patients undergoing elective major abdominal surgery.

Methods

Trial Design and Oversight

The PELICAN trial was a multicenter, single-blind, superiority randomized clinical trial conducted at 12 university medical centers in Austria, the Czech Republic, Denmark, Germany, and Spain. The trial protocol was published[14] and 4 versions appear in Supplements 1-4. Protocol version 1.2 was the first complete protocol version and the one initially approved by the ethics committee. The statistical analysis plan (finalized on March 20, 2026) appears in Supplement 5. The trial was approved by the Hamburg ethics committee and by the ethics committee at each site. All patients provided written informed consent. An independent data and safety monitoring board provided trial oversight and reviewed the results of a planned interim analysis.

In the interim analysis (completed on June 30, 2025), the composite primary outcome occurred in 119 of 283 patients (42.0%) in the individualized cardiac index-guided hemodynamic therapy group vs 138 of 281 patients (49.1%) in the routine hemodynamic therapy group; the 1-sided *P* value was .046. The trial followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.[15]

Patient Population

We included patients who were 45 years of age or older, were scheduled to undergo elective major abdominal surgery (involving visceral organs) under general anesthesia with an expected duration of surgery of 90 minutes or longer, and who had at least 1 high-risk criterion (eMethods in Supplement 6). High-risk criteria were patient-related or surgery-related factors increasing the risk of developing postoperative complications.[7,16]

We excluded patients (1) undergoing ambulatory surgery, nephrectomy, or liver or kidney transplant surgery; (2) with prior transplant of the kidney, liver, heart, or lung; (3) with sepsis; (4) who were classified as having American Society of Anesthesiologists physical status V or VI; (5) who were pregnant; and (6) in whom it was impossible to perform cardiac index monitoring. All inclusion and exclusion criteria appear in the eMethods in Supplement 6.

Preoperative Resting and Intraoperative Cardiac Index Measurements

In all patients, preoperative resting cardiac index was measured over a 5-minute period using the noninvasive bioreactance Starling Fluid Management System (Baxter) while the patient was awake and in the supine position. Preoperative measurements were usually performed at least 1 day before surgery, and occasionally on the day of surgery. In patients with a preoperative resting cardiac index less than 2.2 L/min/m^2, a value of 2.2 L/min/m^2 was assigned. During surgery, cardiac index also was measured with the bioreactance system.

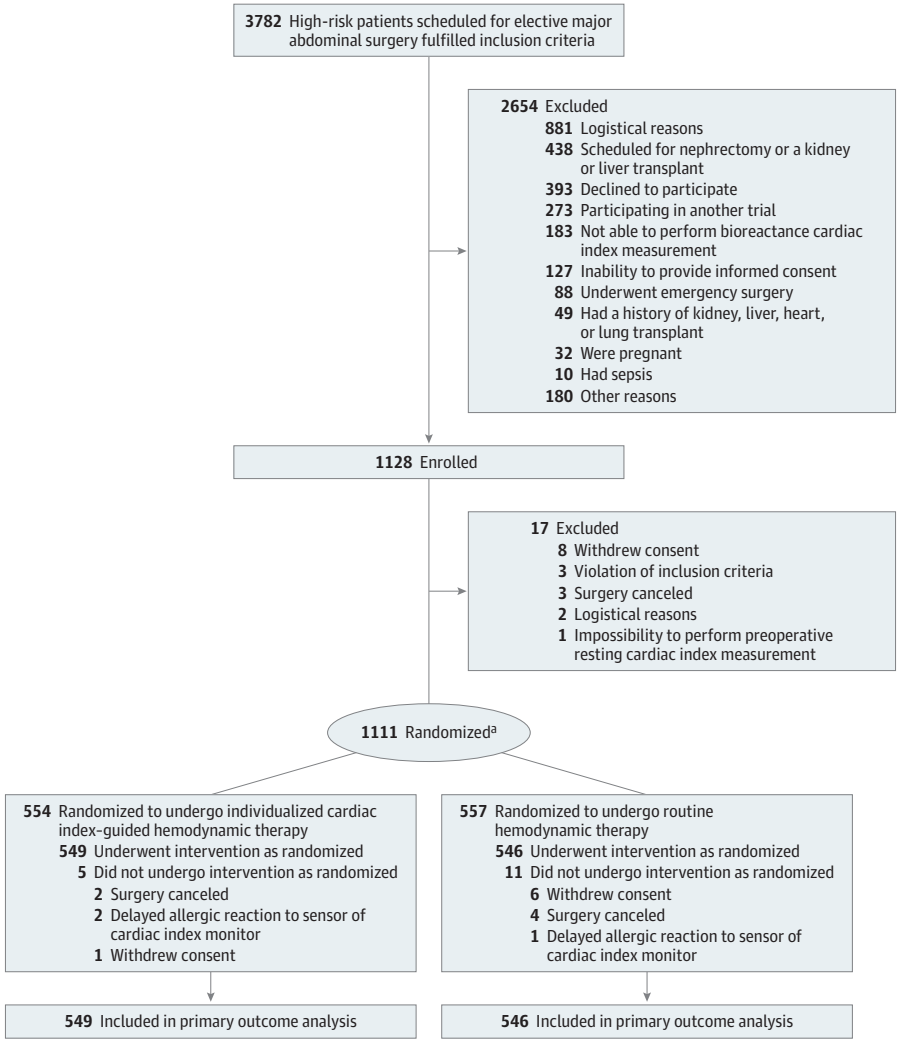
Randomization and Treatment

Patients were randomized using an online system in a 1:1 ratio using central block-wise randomization with variable block lengths (block sizes of 4 and 6) to individualized cardiac index-guided hemodynamic therapy (intervention group) or routine hemodynamic therapy (with blinded cardiac index monitoring; control group) (**Figure 1**). Randomization was stratified by center.

In both groups, clinicians strove to maintain mean arterial pressure above 65 mm Hg. For the patients in the individualized cardiac index-guided hemodynamic therapy group, clinicians were instructed to maintain intraoperative cardiac index at least equal to the patient's preoperative resting cardiac index from surgical incision to the end of surgery by

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Figure 1. Flow Diagram Depicting Enrollment and Randomization of the Participants



[a]Randomization was stratified by center.

administering balanced crystalloids at a baseline infusion rate of 6 mL/kg/h, additional 500-mL fluid boluses, and dobutamine according to a treatment algorithm (eMethods in Supplement 6). For patients in the routine hemodynamic therapy group, hemodynamic management was performed at the discretion of the anesthesiologist. Clinicians were not aware of the patient's resting cardiac index and were blinded to intraoperative cardiac index measurements.

Outcomes

The primary outcome was the incidence of a composite outcome of acute kidney injury, acute myocardial injury (including myocardial infarction), severe infectious complications, nonfatal cardiac arrest, or death within the first 7 postoperative days. *Acute kidney injury* was defined as an increase in serum creatinine of 50% or greater from baseline or need for kidney replacement therapy.[17] *Acute myocardial injury* was defined as an increase in high-sensitivity troponin according to the published definition[18] of "myocardial injury and infarction associated with non-cardiac procedures." *Severe infectious complications* were defined according to the published definition[19] and included fever, respiratory infection, neurological infection, urinary system infection, colitis or infection with *Clostridioides difficile*, endometritis, surgical site infection, deep incisional surgical site infection, organ or space surgical site infection (including anastomotic leakage), unknown infection with pathogenic organisms in tissue or fluid, and sepsis. *Nonfatal cardiac arrest* was defined as successful resuscitation from either documented or presumed ventricular fibrillation, sustained ventricular tachycardia, asystole, or pulseless electrical activity requiring cardiopulmonary resuscitation, pharmacological therapy, or cardiac defibrillation. *Death* was defined as all-cause mortality.

Baseline and postoperative creatinine and troponin levels were measured systematically as part of the trial. Acute kidney injury and acute myocardial injury were determined centrally by applying the prespecified criteria to these laboratory data. Severe infectious complications, nonfatal cardiac arrest, and death were assessed by dedicated research personnel at each center.

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The secondary outcomes included the incidence of the composite primary outcome within the first 3 postoperative days; the incidence of the individual components of the primary outcome within the first 3 and 7 postoperative days; the incidence of individual infectious complications within the first 7 postoperative days; the collapsed incidence and each individual incidence of need for kidney replacement therapy, myocardial infarction, nonfatal cardiac arrest, or death within the first 30 and 90 postoperative days; the time to transfer from the intensive care unit to the general ward within the first 90 postoperative days; the time to hospital discharge within the first 90 postoperative days; and the incidence of unplanned hospital readmission within the first 30 postoperative days. A complete list of outcome definitions appears in the eMethods in Supplement 6.

Statistical Analysis

For the sample size calculation, we assumed an incidence of the composite primary outcome of 45% in patients assigned to routine hemodynamic therapy and of 35% in patients assigned to individualized cardiac index-guided hemodynamic therapy (based on our own pilot trial,[13] a previous multicenter trial,[20] and a trial protocol[21]).

We used a group-sequential design with one planned interim analysis after enrollment of 50% of the patients, using the O'Brien-Fleming α spending function.[22] A total sample size of 1014 patients (507 per group) was required to achieve 90% power to detect an absolute difference of 10% in the incidence of the primary outcome between patients in the individualized cardiac index-guided hemodynamic therapy group vs patients in the routine hemodynamic therapy group at a global significance level of 5% using a 2-sided test of proportions without continuity correction and considering the interim analysis. Accounting for an expected total dropout rate of 10%, we planned to enroll 1128 patients (564 per group).

The primary and secondary outcomes were analyzed in the modified intention-to-treat population, which included all patients who consented, were randomized, and underwent surgery. The primary outcome was fully observed for all patients in the modified intention-to-treat population. For the secondary outcomes with missing data, an analysis of available cases was performed to maintain the largest possible sample size.

The final primary outcome analysis was conducted using a 2-sided test of proportions without continuity correction at a significance level of .049. The risk difference and the relative risk with 2-sided 95.1% CI were calculated. As sensitivity analysis, the primary outcome was analyzed using a mixed-effects logistic regression model including a fixed effect for the randomized treatment group and a random intercept for center to account for the cluster structure in the data.

Categorical secondary outcomes were analyzed using 2-sided tests of proportions without continuity correction or Fisher exact tests depending on the expected cell counts. Time-to-event outcomes were assessed using Aalen-Johansen estimators, Gray tests, and cause-specific Cox regression analyses to account for death as a competing event. The analyses of the secondary outcomes were exploratory and performed without adjustment for multiplicity.

The analyses of the primary and secondary outcomes were repeated in the per-protocol population, excluding patients assigned to individualized cardiac index-guided hemodynamic therapy who had major protocol violations. Prespecified subgroup analyses were performed for age, sex, American Society of Anesthesiologists physical status, preoperative resting cardiac index, surgical technique, and duration of surgery. These analyses were performed using mixed-effects logistic regression models including treatment group, subgroup, and a treatment × subgroup interaction as fixed effects and center as a random effect. All analyses were performed using R version 4.5.0 (R Foundation for Statistical Computing).

Results

Patients

Between October 8, 2023, and October 25, 2025, 1128 patients were enrolled and 1111 patients were randomized (554 patients [49.9%] in the individualized cardiac index-guided hemodynamic therapy group vs 557 patients [50.1%] in the routine hemodynamic therapy group; Figure 1). Of the 1111 patients randomized, 16 were excluded after randomization (most commonly because of withdrawal of consent or cancellation of surgery). A total of 1095 patients were included in the modified intention-to-treat analysis; 549 (50.1%) in the individualized cardiac index-guided hemodynamic therapy group vs 546 (49.9%) in the routine hemodynamic therapy group. Primary outcome data were available for all 1095 patients. The baseline patient characteristics were similar between the groups (**Table 1**). Additional information appears in the eResults in Supplement 6. The date of last follow-up was January 15, 2026.

Preoperative Resting Cardiac Index

The median preoperative resting cardiac index was 2.9 L/min/m^2 (IQR, 2.6-3.3 L/min/m^2; range, 2.2-5.0 L/min/m^2) among patients in the individualized cardiac index-guided hemodynamic therapy group vs 2.9 L/min/m^2 (IQR, 2.5-3.3 L/min/m^2; range, 2.2-4.9 L/min/m^2) among patients in the routine hemodynamic therapy group (eFigure 1 in Supplement 6).

Intraoperative Management and Cardiac Index

Patients in the individualized cardiac index-guided hemodynamic therapy group were given higher total volumes of intravenous fluids (3500 mL [IQR, 2369-5450 mL]) than patients in the routine hemodynamic therapy group (2838 mL [IQR, 1696-4130 mL]; **Table 2**). In addition, the proportion of patients given dobutamine was substantially higher in the individualized cardiac index-guided hemodynamic therapy group (351/548 [64.1%]) than in the routine hemodynamic therapy group (3/546 [0.5%]).

The median average intraoperative cardiac index was 3.1 L/min/m^2 (IQR, 2.6-3.6 L/min/m^2; range, 1.5-6.6 L/min/m^2) among patients in the individualized cardiac index-guided hemodynamic therapy group vs 2.7 L/min/m^2 (IQR, 2.2-3.1 L/min/m^2; range, 0.9-4.7 L/min/m^2) among patients in the routine hemodynamic therapy group (**Figure 2**A). The median

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Table 1. Baseline Patient Characteristics

Characteristic	Hemodynamic therapy, No. (%)[a]	
	Individualized cardiac index-guided (n = 549)	Routine (n = 546)
Age, median (IQR), y	67 (59-74)	66 (59-74)
Sex		
Female	267 (48.6)	274 (50.2)
Male	282 (51.4)	272 (49.8)
Height, median (IQR), cm	172 (165-179)	172 (165-180)
Weight, median (IQR), kg	75 (65-88)	75 (64-89)
Body mass index, median (IQR)[b]	25.5 (22.8-28.4)	25.2 (22.1-28.7)
American Society of Anesthesiologists physical status		
Healthy (grade I)	16 (2.9)	20 (3.7)
Mild systemic disease (grade II)	205 (37.3)	204 (37.4)
Severe systemic disease (grade III)	316 (57.6)	313 (57.3)
Life-threatening severe systemic disease (grade IV)	12 (2.2)	9 (1.6)
Other comorbidities and coexisting conditions		
Solid organ cancer	436 (79.4)	442 (81.0)
Chronic arterial hypertension	284 (51.7)	277 (50.7)
Atrial fibrillation	45 (8.2)	53 (9.7)
Hematological malignancies	11 (2.0)	6 (1.1)
Medications		
Statin therapy	166 (30.2)	133 (24.4)
Oral anticoagulation therapy	87 (15.8)	89 (16.3)
Aspirin therapy	68 (12.4)	69 (12.6)
High-risk criteria		
Expected surgery duration ≥3 h	441 (80.3)	452 (82.8)
Aged ≥65 y	308 (56.1)	300 (54.9)
Kidney impairment	302 (55.0)	295 (54.0)
Body mass index ≥30[b]	106 (19.3)	117 (21.4)
History of smoking within past 2 y	94 (17.1)	120 (22.0)
Diabetes requiring medication	90 (16.4)	70 (12.8)
Immunodeficiency due to a disease or therapy	64 (11.7)	61 (11.2)
Coronary artery disease	37 (6.7)	41 (7.5)
COPD or pulmonary fibrosis	37 (6.7)	41 (7.5)
Exercise tolerance <4 metabolic equivalents	34 (6.2)	35 (6.4)
History of stroke	27 (4.9)	27 (4.9)
Chronic heart failure	19 (3.5)	21 (3.8)
Valvular heart disease	17 (3.1)	22 (4.0)
Peripheral arterial occlusive disease	16 (2.9)	18 (3.3)
Liver cirrhosis	15 (2.7)	9 (1.6)
B-type natriuretic peptide level >80 ng/L or NT-proBNP level >200 ng/L within the last 6 mo	8 (1.5)	9 (1.6)
Preoperative resting cardiac index, median (IQR), L/min/m^2	2.9 (2.6-3.3)	2.9 (2.5-3.3)

Abbreviations: COPD, chronic obstructive pulmonary disease; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

[a] Some data are expressed as median (IQR) as indicated in the rows.

[b] Calculated as weight in kilograms divided by height in meters squared.

percentage of time that intraoperative cardiac index was at least equal to the preoperative resting cardiac index was 62% (IQR, 32%-83%) among patients in the individualized cardiac index-guided hemodynamic therapy group vs 23% (IQR, 2%-66%) among patients in the routine hemodynamic therapy group (Figure 2B). The median area under the preoperative resting cardiac index was 25 L/min/m^2 × min (IQR, 8-62 L/min/m^2 × min) among patients in the individualized cardiac index-guided hemodynamic therapy group vs 70 L/min/m^2 × min (IQR, 19-182 L/min/m^2 × min) among patients in the routine hemodynamic therapy group (Figure 2C and eFigure 2 in Supplement 6).

Primary Outcome

In the modified intention-to-treat analysis, the primary outcome occurred in 243 of 549 patients (44.3%) in the individualized cardiac index-guided hemodynamic therapy group vs

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Table 2. Surgical and Anesthetic Characteristics

Characteristic	Hemodynamic therapy, No. (%)[a]	
	Individualized cardiac index-guided (n = 549)	Routine (n = 546)
Type of surgery		
General	397 (72.3)	404 (74.0)
Gynecological	55 (10.0)	63 (11.5)
Liver	57 (10.4)	50 (9.2)
Urological	40 (7.3)	29 (5.3)
Time from randomization to start of surgery, median (IQR), min	156 (99-928)	153 (96-948)
Duration of surgery, median (IQR), min	215 (155-307)	225 (160-302)
Postoperative care		
General ward	258 (47.0)	246 (45.1)
Intermediate care unit	102 (18.6)	109 (20.0)
Intensive care unit	189 (34.4)	191 (35.0)
Anesthetic technique		
Total intravenous anesthesia	307 (55.9)	318 (58.2)
Balanced anesthesia[b]	242 (44.1)	228 (41.8)
Epidural block	280 (51.0)	316 (57.9)
Intra-arterial blood pressure monitoring (arterial catheter)	411 (74.9)	418 (76.6)
Fluids		
Total fluid volume, median (IQR), mL	3500 (2369-5450)	2838 (1696-4130)
Crystalloids, median (IQR), mL	3302 (2107-4578) [n = 547]	2500 (1541-3750) [n = 543]
Use of albumin	124 (22.6)	94 (17.2)
Albumin, median (IQR), mL	500 (250-1000) [n = 124]	500 (250-938) [n = 94]
Use of synthetic colloids	117 (21.3)	89 (16.3)
Synthetic colloids, median (IQR), mL	1000 (500-1000) [n = 117]	500 (500-1000) [n = 89]
Blood products		
Use of packed red blood cells	82 (14.9)	59 (10.8)
Packed red blood cells, median (IQR), mL	550 (280-1060) [n = 82]	560 (280-1040) [n = 59]
Use of fresh frozen plasma	53 (9.7)	41 (7.5)
Fresh frozen plasma, median (IQR), mL	1160 (750-1800) [n = 53]	900 (750-1500) [n = 41]
Catecholamines		
Use of norepinephrine, No./total (%)	434/548 (79.2)	418/546 (76.6)
Norepinephrine, median (IQR), mg	1.44 (0.70-3.41) [n = 434]	2.14 (0.95-3.63) [n = 418]
Use of dobutamine, No./total (%)	351/548 (64.1)	3/546 (0.5)
Dobutamine, median (IQR), mg	35.0 (17.9-69.0) [n = 351]	11.9 (7.6-44.0) [n = 3]
Use of ephedrine, No./total (%)	121/548 (22.1)	136/546 (24.9)
Ephedrine, median (IQR), mg	20 (10-20) [n = 121]	15 (10-21) [n = 136]
Use of phenylephrine, No./total (%)	124/548 (22.6)	107/546 (19.6)
Phenylephrine, median (IQR), mg	1.00 (0.40-4.00) [n = 124]	2.10 (0.40-5.10) [n = 107]
Use of epinephrine, No./total (%)	10/548 (1.8)	14/546 (2.6)
Epinephrine, median (IQR), µg	296 (184-406) [n = 10]	165 (44-590) [n = 14]
Intraoperative hemodynamic measures, median (IQR)[c]		
Average cardiac index, L/min/m^2	3.1 (2.6-3.6) [n = 542]	2.7 (2.2-3.1) [n = 540]
Average stroke volume index, mL/m^2	43 (35-50) [n = 542]	40 (34-48) [n = 540]
Average heart rate, beats/min	72 (64-82) [n = 542]	65 (58-75) [n = 540]

[a] Some data are expressed as median (IQR) or No./total (%) as indicated in the rows. All data on administered medications (including fluids, blood products, and catecholamines) and the hemodynamic data refer exclusively to the intervention period (from surgical incision to the end of surgery).

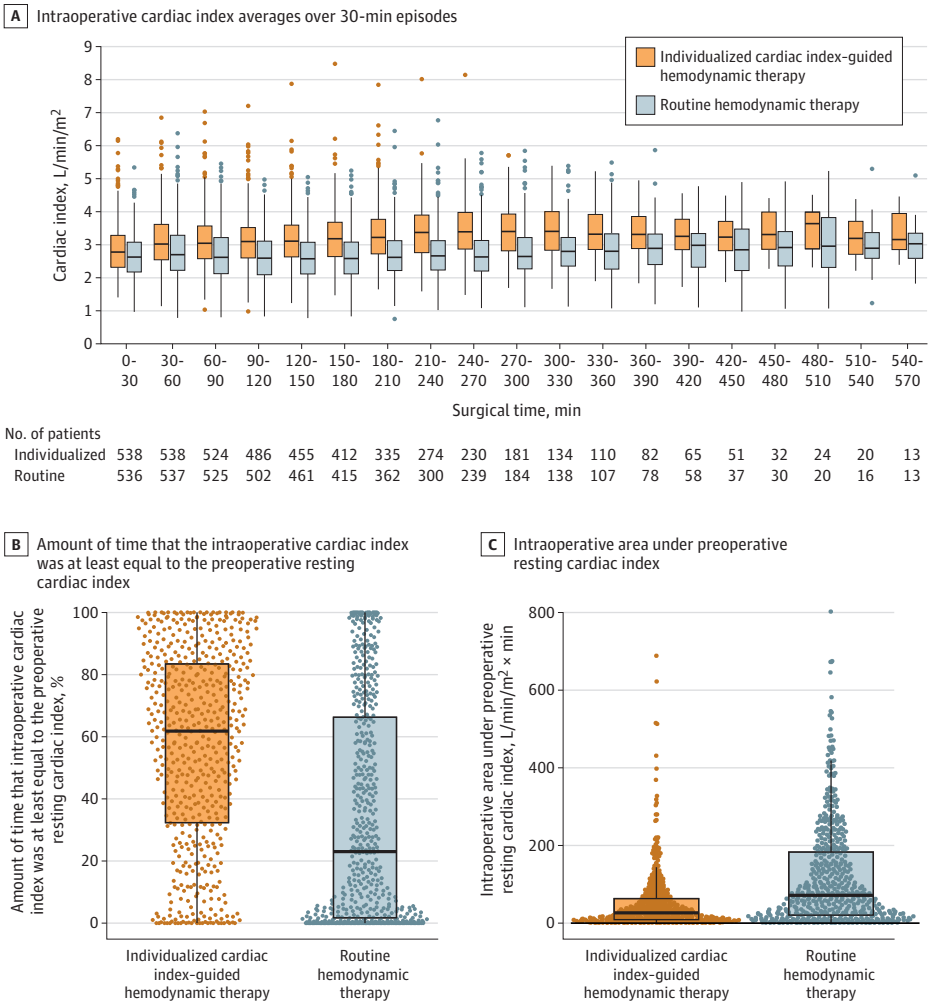
[b] Refers to general anesthesia maintained with a volatile (inhalational) anesthetic agent combined with intravenous opioids.

[c] Recorded in both groups; however, in the routine hemodynamic therapy group, clinicians were blinded to assessments of intraoperative cardiac index and stroke volume index.

256 of 546 patients (46.9%) in the routine hemodynamic therapy group (relative risk, 0.94 [95.1% CI, 0.83-1.08]; P = .38) (**Table 3**). After accounting for center effects in a mixed-effects logistic regression model, the adjusted odds ratio was 0.89 (95% CI, 0.70-1.14; P = .37; intraclass correlation coefficient = 0.11) (eFigure 3 in Supplement 6).

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Figure 2. Box-and-Whisker Plots Depicting the Separation of the Intraoperative Cardiac Index Between Groups



The boxes represent the 25th and 75th percentiles and the horizontal bold lines inside the boxes represent median values. The whiskers indicate the lowest and highest value no further than 1.5 times the IQR. Intraoperative cardiac index data were available for 1082 of 1095 patients (542 of 549 patients in the individualized cardiac index–guided hemodynamic therapy group and 540 of 546 patients in the routine hemodynamic therapy group); missing values were not imputed.

A, Intraoperative cardiac index averages over 30-min episodes (censored after 9.5 hours).

B, The box plots with overlaying 1-dimensional scatter plots illustrate the percentage of time that the intraoperative cardiac index was at least at the preoperative resting cardiac index.

C, The box plots with overlaying 1-dimensional scatter plots illustrate the intraoperative area under the preoperative resting cardiac index. The area under preoperative resting cardiac index quantifies both how long and to what extent intraoperative cardiac index was below a patient's preoperative resting cardiac index (eFigure 2 in Supplement 6). The smaller the area under the preoperative resting cardiac index, the shorter the duration or the smaller the extent to which the intraoperative cardiac index was below the patient's preoperative resting cardiac index.

In 2 patients (0.4%) in the individualized cardiac index-guided hemodynamic therapy group, the preoperative resting cardiac index was assessed incorrectly. There were 15 patients (2.7%) in whom clinicians did not start or discontinued the trial intervention. Therefore, the per-protocol population included 1078 patients; 532 (49.4%) in the individualized cardiac index-guided hemodynamic therapy group vs 546 (50.6%) in the routine hemodynamic therapy group. In the per-protocol analysis, the primary outcome occurred in 235 of 532 patients (44.2%) in the individualized cardiac index-guided hemodynamic therapy group vs 256 of 546 patients (46.9%) in the routine hemodynamic therapy group (relative risk, 0.94 [95.1% CI, 0.83-1.07]; P = .37). Individualized cardiac index-guided hemodynamic therapy did not reduce the risk for the primary composite outcome in any of the prespecified subgroups (eTable 1 in Supplement 6).

Secondary Outcomes

The secondary outcomes appear in Table 3 (additional data appear in eTable 2 and eFigures 4-6 in Supplement 6). The proportion of patients who died within the first 90 postoperative days was higher in the individualized cardiac index-guided hemodynamic therapy group (31/541 [5.7%]) than in the routine hemodynamic therapy group (15/540 [2.8%]) (relative risk, 2.06 [95% CI, 1.13-3.78]) (eTable 3 and eFigure 6 in Supplement 6). There were no differences in any other secondary outcome, including the incidence of a composite outcome of need for kidney replacement therapy, myocardial infarction, nonfatal cardiac arrest, or death within the first 30 and 90 postoperative days and the incidence of unplanned hospital readmission within the first 30 postoperative days.

Discussion

In this multicenter trial, individualized cardiac index-guided hemodynamic therapy targeting the patient's preoperative resting cardiac index did not significantly reduce the incidence of a composite primary outcome of acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death within the first 7 postoperative days compared with routine hemodynamic therapy

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Table 3. Primary and Secondary Outcomes

	Hemodynamic therapy, No. (%)[a]			
	Individualized cardiac index–guided (n = 549)	Routine (n = 546)	Absolute difference (95% CI), %	Relative risk (95% CI)
Primary composite outcome within the first 7 postoperative days				
Acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death	243 (44.3)	256 (46.9)	−2.6 (−8.5 to 3.3)[b]	0.94 (0.83 to 1.08)[b,c]
Secondary outcomes within the first 7 postoperative days				
Elements of the primary composite outcome				
Acute kidney injury, No./total (%)	52/544 (9.6)	70/540 (13.0)	−3.4 (−7.2 to 0.4)	0.74 (0.53 to 1.03)
Acute myocardial injury, No./total (%)	158/531 (29.8)	164/525 (31.2)	−1.5 (−7.0 to 4.1)	0.95 (0.79 to 1.14)
Severe infectious complications	116 (21.1)	115 (21.1)	0.1 (−4.8 to 4.9)	1.00 (0.80 to 1.26)
Nonfatal cardiac arrest	1 (0.2)	3 (0.5)	−0.4 (−1.1 to 0.3)	0.33 (0.03 to 3.18)
Death	3 (0.5)	3 (0.5)	0 (−0.9 to 0.9)	0.99 (0.20 to 4.91)
Elements of severe infectious complications				
Fever	23 (4.2)	19 (3.5)	0.7 (−1.6 to 3.0)	1.20 (0.66 to 2.18)
Respiratory infection	19 (3.5)	12 (2.2)	1.3 (−0.7 to 3.2)	1.57 (0.77 to 3.21)
Neurological infection	0	1 (0.2)		
Urinary system infection	26 (4.7)	22 (4.0)	0.7 (−1.7 to 3.1)	1.18 (0.67 to 2.05)
Colitis or infection with *Clostridioides difficile*	3 (0.5)	1 (0.2)	0.4 (−0.4 to 1.1)	2.98 (0.31 to 28.59)
Endometritis	0	0		
Surgical site infection	17 (3.1)	15 (2.7)	0.3 (−1.6 to 2.3)	1.13 (0.57 to 2.23)
Deep incisional surgical site infection	9 (1.6)	7 (1.3)	0.4 (−1.1 to 1.8)	1.28 (0.48 to 3.41)
Organ or space surgical site infection	32 (5.8)	27 (4.9)	0.9 (−1.8 to 3.6)	1.18 (0.72 to 1.94)
Unknown infection with pathogenic organisms in tissue or fluid	70 (12.8)	65 (11.9)	0.8 (−3.0 to 4.7)	1.07 (0.78 to 1.47)
Sepsis	19 (3.5)	15 (2.7)	0.7 (−1.3 to 2.8)	1.26 (0.65 to 2.45)
Secondary outcomes within the first 3 postoperative days				
Composite outcome[d]	194 (35.3)	213 (39.0)	−3.7 (−9.4 to 2.0)	0.91 (0.78 to 1.06)
Elements of composite outcome				
Acute kidney injury, No./total (%)	40/544 (7.4)	58/540 (10.7)	−3.4 (−6.8 to 0)	0.68 (0.47 to 1.01)
Acute myocardial injury, No./total (%)	141/531 (26.6)	149/525 (28.4)	−1.8 (−7.2 to 3.6)	0.94 (0.77 to 1.14)
Severe infectious complications	59 (10.7)	59 (10.8)	−0.1 (−3.7 to 3.6)	0.99 (0.71 to 1.40)
Nonfatal cardiac arrest	0	2 (0.4)		
Death	1 (0.2)	2 (0.4)	−0.2 (−0.8 to 0.4)	0.50 (0.05 to 5.47)
Secondary outcomes within the first 30 postoperative days				
Composite outcome,[e] No./total (%)	22/547 (4.0)	18 (3.3)	0.7 (−1.5 to 3.0)	1.22 (0.66 to 2.25)
Elements of composite outcome, No./total (%)				
Need for kidney replacement therapy	7/545 (1.3)	11/545 (2.0)	−0.7 (−2.2 to 0.8)	0.64 (0.25 to 1.63)
Myocardial infarction	1/544 (0.2)	2/543 (0.4)	−0.2 (−0.8 to 0.4)	0.50 (0.05 to 5.49)
Nonfatal cardiac arrest	4/544 (0.7)	5/545 (0.9)	−0.2 (−1.3 to 0.9)	0.80 (0.22 to 2.97)
Death	16/547 (2.9)	8 (1.5)	1.5 (−0.3 to 3.2)	2.00 (0.86 to 4.63)
Unplanned hospital readmission	65 (11.8)	63 (11.5)	0.3 (−3.5 to 4.1)	1.03 (0.74 to 1.42)
Secondary outcomes within the first 90 postoperative days[f]				
Composite outcome,[g] No./total (%)	35/541 (6.5)	25/540 (4.6)	1.8 (−0.9 to 4.6)	1.40 (0.85 to 2.30)
Elements of composite outcome, No./total (%)				
Need for kidney replacement therapy	9/528 (1.7)	11/537 (2.0)	−0.3 (−2.0 to 1.3)	0.83 (0.35 to 1.99)
Myocardial infarction	3/526 (0.6)	2/533 (0.4)	0.2 (−0.6 to 1.0)	1.52 (0.26 to 9.06)
Nonfatal cardiac arrest	4/526 (0.8)	7/534 (1.3)	−0.6 (−1.8 to 0.7)	0.58 (0.17 to 1.97)
Death	31/541 (5.7)	15/540 (2.8)	3.0 (0.6 to 5.4)	2.06 (1.13 to 3.78)
Intensive care unit length of stay, median (IQR), d[h]	1 (1 to 3)	1 (1 to 3)		
Hospital length of stay, median (IQR), d[h]	8 (5 to 15)	9 (5 to 16)		

[a] Some data are expressed as No./total (%) or median (IQR) as indicated.

[b] The data in parentheses are a 95.1% CI.

[c] $P = .38$ for between-group comparison.

[d] Acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death.

[e] Need for kidney replacement therapy (KRT), myocardial infarction (MI), nonfatal cardiac arrest, or death.

[f] Additional secondary outcomes appear in eFigures 4-5 in Supplement 6.

[g] Need for KRT, MI, nonfatal cardiac arrest, or death.

[h] Censored at postoperative day 90 or death.

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in high-risk patients undergoing elective major abdominal surgery.

The incidence of 90-day mortality was higher in the individualized cardiac index-guided therapy group. Because this was one of multiple secondary outcomes and no adjustment for multiple testing was performed, the finding should be interpreted cautiously. It may represent a chance finding or a potential adverse effect of the intervention.

The evidence for the effect of intraoperative cardiac index-guided hemodynamic therapy on outcomes in patients undergoing elective abdominal surgery is controversial. Numerous small (mostly conducted at a single center) trials have suggested that intraoperative cardiac index–guided hemodynamic therapy may improve patient-centered outcomes.[23] However, these beneficial effects suggested by small trials could not be replicated in larger, multicenter trials.[24] The 734-patient OPTIMISE trial[20] was underpowered to definitively determine whether the observed reduction in the incidence of the composite outcome of complications (43% with routine care vs 37% with cardiac output–guided hemodynamic therapy) represented a true clinically important effect because the result did not reach statistical significance (relative risk, 0.84 [95% CI, 0.71-1.01]; $P = .07$). In the subsequent 2498-patient OPTIMISE II trial,[11] cardiac output–guided fluid therapy with low-dose inotrope infusion did not reduce the incidence of a composite outcome of infectious complications compared with routine care (23% vs 23%; adjusted odds ratio, 1.03 [95% CI, 0.84-1.25]; $P = .81$). In the 364-patient iPEGASUS trial,[12] cardiac index–guided hemodynamic therapy even increased the incidence of a composite outcome of complications within 28 days after surgery compared with routine care (55% vs 46%, respectively; odds ratio, 1.87 [95% CI, 1.03-3.39]; $P = .04$).

This trial conceptually differs from previous multicenter trials and extends them by individualizing intraoperative cardiac index targets based on each patient's preoperative resting cardiac index. Defining target values is a fundamental element of cardiac index–guided hemodynamic therapy. Different target definitions rely on different pathophysiological assumptions and lead to substantially different cardiac index target values.[25] Previous multicenter trials either used fixed cardiac index targets[26] or aimed to maximize cardiac index after induction of general anesthesia and maintain this maximized postinduction value throughout surgery.[11,12,20] Although it is reasonable to assume that maximizing cardiac index may help protect organs from tissue hypoperfusion and hypoxia, this strategy may also lead to overtreatment with fluids and inotropes, potentially causing acute cardiac events and other complications.[11,12] Instead of maximizing cardiac index, intraoperative cardiac index was maintained at the individual preoperative resting cardiac index in this trial. The rationale for this approach was 2-fold. First, preoperative cardiac index varies considerably among patients presenting for elective surgery.[13] Second, maintaining the preoperative resting cardiac index may ensure adequate tissue perfusion and oxygenation during surgery with general anesthesia—when energy expenditure is lower than awake resting energy expenditure.[27]

The main hemodynamic target was cardiac index (the product of heart rate and stroke volume index). The trial intervention (mainly administration of fluids and dobutamine) did increase both heart rate and stroke volume index. Compared with patients in the routine hemodynamic therapy group, the median intraoperative average heart rate was approximately 11% higher and the median intraoperative stroke volume index was approximately 7% higher in patients in the individualized cardiac index-guided hemodynamic therapy group.

There were only few protocol violations. The median intraoperative cardiac index and the proportion of time that intraoperative cardiac index was at least equal to the preoperative resting cardiac index were markedly higher in patients in the individualized cardiac index-guided hemodynamic therapy group than in patients in the routine hemodynamic therapy group. Nevertheless, maintaining preoperative resting cardiac index during surgery did not translate into improved patient-centered outcomes.

There are several potential explanations for this finding. The overarching premise of preventing organ injury through intraoperative cardiac index-guided hemodynamic therapy is that increasing cardiac index increases oxygen delivery and, thereby, ensures that tissue perfusion and oxygenation meet metabolic demands.[1,3] However, increasing cardiac index does not necessarily result in increased oxygen delivery. The administration of intravenous fluids may cause hemodilution, which can reduce arterial oxygen content despite an increase in cardiac index.[28,29] Furthermore, increasing oxygen delivery can improve tissue oxygenation only when oxygen consumption becomes dependent on oxygen delivery.

However, contemporary surgical and anesthetic care—including minimally invasive surgical techniques, mechanical ventilation, blood transfusion strategies, and general anesthesia (which reduces energy expenditure and oxygen consumption[27])—may prevent oxygen consumption from becoming dependent on oxygen delivery. In addition, we used a pragmatic hemodynamic treatment algorithm to guide the administration of fluids and dobutamine in patients in the individualized cardiac index-guided hemodynamic therapy group. The substantial variability in the patients' baseline risk, comorbidities, physiological reserve, and responses to anesthesia and surgical trauma may also limit the effectiveness of a standardized hemodynamic treatment protocol.

Limitations

This trial has several limitations. First, we did not measure arterial oxygen content and oxygen delivery, which limits our ability to evaluate the direct relationship between cardiac index and tissue perfusion and oxygenation.

Second, the trial population consisted of patients undergoing elective major abdominal surgery. The findings, therefore, cannot be generalized to patients undergoing other types of surgery or emergency surgery.

Third, the trial was conducted at university medical centers with experience in intraoperative cardiac index monitoring, which may not reflect practice in smaller hospitals or at centers with less hemodynamic monitoring expertise.

Fourth, we assessed preoperative resting and intraoperative cardiac index using a bioreactance method. The bioreactance method has been validated against reference methods in experimental and clinical settings,[30-33] but is not a clinical

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reference method. However, because bioreactance was used for both the preoperative and intraoperative cardiac index measurements, the intervention relied more on the within-patient consistency than on absolute accuracy.

Fifth, we focused primarily on complications occurring within the first 7 postoperative days to reduce confounding by postoperative events unrelated to surgery and intraoperative management. However, this approach may have missed later complications. To address this, we included secondary analyses of complications occurring within 30 and 90 days after surgery to capture longer-term outcomes.

Conclusions

Among high-risk patients undergoing elective major abdominal surgery, individualized cardiac index-guided hemodynamic therapy targeting the patient's preoperative resting cardiac index did not reduce the incidence of a composite outcome of acute kidney injury, acute myocardial injury, severe infectious complications, nonfatal cardiac arrest, or death within the first 7 postoperative days compared with routine hemodynamic therapy.

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