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ORIGINAL ARTICLE

Impact of intraoperative hypotension on hospital stay in major abdominal surgery

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Abstract

Purpose Although the relationship between preoperative risk factors and outcomes has been extensively studied, the effect of intraoperative hemodynamic changes in a patient's postoperative course has been less well defined.

Methods We designed a prospective observational study to assess the impact of several variables, and especially hypotension, on postoperative outcome. Patients considered eligible for the study, all more than 18 years old, were mentally stable patients scheduled for major abdominal surgery with an expected duration of more than 2 h. Total hypotension time (THT), with other variables that possibly influence the outcome, was analyzed using multivariate logistic regression analysis in 100 consecutive patients.

Results Total hypotension time was isolated as a factor significantly associated with morbidity [odds ratio, 5.1 (1.95–13.35)] and significantly prolonged hospital stay [odds ratio, 4.56 (1.85–10.96)]. Patients who had prolonged THT presented more complications (50 vs. 30), especially of the cardiovascular, pulmonary, and gastrointestinal systems. These complications led to delayed hospital discharge in a significant number of patients (36 with THT vs. 17 others). Finally, duration of surgery was associated with postoperative complications [odds ratio, 3.1 (1.2–8.0)].

Conclusion Persistent hypotension during elective major abdominal surgery is a significant risk factor for postoperative complications and may prolong hospitalization and affect patient outcomes. Anesthetic management for the avoidance of hypotension, as much as possible, during major abdominal surgery may positively affect outcomes.

Keywords Intraoperative hypotension · Major surgery · Outcome · Complications

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Introduction

Perioperative morbidity and mortality are broadly correlated with patient comorbidity, the surgery itself, and anesthetic management [1]. It is well established that patient physical status and increased American Society of Anesthesiologists (ASA) score are in good correlation with the risk of postoperative mortality. Studies suggest that the patient's general condition, especially at the time of admission to the hospital, has the highest impact on outcome. Poor outcome may increase as much as 10% in the elderly and with patients undergoing urgent operations [2–7].

Although anesthetic management is included among the factors affecting perioperative outcome, the risk of anesthesia in the immediate perioperative period for elective cases presently appears to be quite low [8]. Nevertheless, intraoperative hemodynamic changes have been reported as important prognostic factors of morbidity and mortality [1, 5, 9–11]. Evidence shows that hypotension under general anesthesia is associated with adverse outcomes in patients undergoing cardiac and noncardiac surgery [12–15]. It is reported that mortality risk is increased by more than 1% per minute of systolic blood pressure below 80 mmHg [2]. Others, however, have shown that controlled hypotension (mean arterial pressure between 45 and 55 mmHg) was completely safe in elders who suffered from cardiac disease, hypertension, or diabetes mellitus and underwent total hip arthroplasty with epidural anesthesia [16]. In the previous randomized trial of deliberate hypotension, no significant additional morbidity risk at 4 months postoperatively was found. Although various studies have evaluated the relationship between preoperative risk factors and outcomes, the postoperative effect of intraoperative hemodynamic abnormalities has been less well defined [10, 17–19].

To elucidate the role of intraoperative hypotension, we hypothesized that this factor may contribute to complications, prolonged hospital stay, or death, especially under certain demographic or clinical conditions such as advanced age or comorbidity. To test this hypothesis and isolate other variables that may be applicable, we designed a prospective observational study of adult patients undergoing elective abdominal surgery, with an anticipated operation time of more than 2 h, under general anesthesia in combination with epidural analgesia.

Methods

This prospective study was conducted in the University Hospital of Larissa/Greece, after approval from the Institution Ethics committee. Patients scheduled for elective major abdominal surgery with an expected duration of more than 2 h were considered eligible for the study. Patients were enrolled consequently under the inclusion criteria of age more than 18 years and written informed consent. Exclusion criteria were pregnancy and mental instability (inability to comprehend and follow orders). A prospective database was created including standard demographic data as well as clinical information, past medical history, and medication intake. Charlson Comorbidity Index [3], New York Heart Association Functional Class [20], and American Society of Anesthesiologists (ASA) physical status classification were also recorded. On the day before surgery, five consecutive blood pressure measurements with a 10-min interval between them were conducted to obtain a mean baseline pressure for further comparisons. All data were checked for completeness and reliability immediately after collection was ended.

All patients received standard anesthesia and perioperative care. No techniques to induce any kind of hypotension deliberately were applied. Monitoring included five-lead ECG and continuous blood pressure measurement after insertion of an intraarterial catheter. Before surgery, a low thoracic (T9–T12) epidural catheter was placed for the 3 days after surgery. Via this catheter, analgesia was provided incrementally from a solution of 21 ml containing 10 ml 0.7% ropivacaine and 1 ml 50 μg fentanyl in normal saline. Induction to anesthesia was achieved with the administration of 10 μg fentanyl, 1–2 mg midazolam, and 1.5–2 mg/kg propofol and maintenance with 1.1–1.2 minimum alveolar concentration (MAC) of sevoflurane. *cis*-Atracurium facilitated tracheal intubation and maintained neuromuscular blockade.

Perioperative information including type and duration of surgery, anesthetic drugs used (as total dose of local anesthetic), hemodynamic variables, fluid and blood product administration, and urine output was recorded on a standardized data collection sheet. Predetermined interval (epoch) for monitors to calculate mean arterial pressure values (MAP) was 2 min. These values were automatically transferred to a running Excel program in a connected computer, creating a patient database. These data were processed according to the following definitions [21, 22]:

$$\begin{aligned}\text{Hypotension} &= \text{MAP} < 60\,\text{mmHg}\\ &\text{MAP} < 70\,\text{mmHg and MAP decrease}\\ &> 30\%\ \text{compared to baseline value.}\end{aligned}$$

Recording was meticulously inspected for artifact values, which were discarded manually and replaced by corrected values. The summation of low values was recorded as the total hypotension time (THT, in minutes). Patients were also automatically allocated to two groups according to the THT during the procedure: (1) up to 10 min, and (2) more than 10 min total for the whole procedure. The attending anesthesiologist was instructed concerning immediate measures to manage hypotension if it occurred. The value of 28% for hematocrit was set as the lowest level for the decision to transfuse packed red cells. The attending anesthesiologist was free to transfuse packed red cells in case of blood loss or in patients whose medical history in relationship to perioperative anemia could lead to complications. Postoperatively, if not contraindicated, invasive hemodynamic monitoring was stopped before post-anesthesia care unit (PACU) discharge. Patients were divided as above considering that limited periods of hypotension during major surgery are not uncommon (for example, hypotension during induction to anesthesia). The surgical team was unaware of the patient's classification for intraoperative hypotension to avoid any bias in postoperative patient care and discharge management.

During the early postoperative period, patients did not expect any oral intake. Depending on the surgeon's decision, they were gradually allowed to take liquids orally and finally to consume food. If this was not possible, they were given parenteral nutrition to avoid starvation. Patients were evaluated daily until discharge. Postoperative information including analgesic requirements, patient sedation, nausea or vomiting (i.e., the number of days that a patient had these symptoms), itching, patient mobilization, oral intake, catheter removal, complications, drugs and fluids administered or lost, and sleep disturbances was recorded on standardized data sheets.

Designing the study, we had to define clear cutoff points between normal and delayed discharge. A retrospective analysis implicating a period of 6 months for these types of procedures revealed that patients without complications and a normal course of healing had left the hospital in 9 days or fewer. To minimize subjectivity for weighting a complication, we analyzed its duration and impact on hospital stay. A patient who was able to leave the hospital in 9 days or fewer had only one or a few minor complications that had not exceeded 4 days. A patient who suffered from a number of different subtle or important complications during the postoperative period required delayed discharge.

For our prospective observation, complications were defined by the need for some specific acute medical therapy or intervention and were entered in the data sheet by title and duration in days (e.g., fever for 1 day). The patients were separated depending on whether they had complications after surgery. Those with complications were further divided in two subgroups according to the number of days presenting with complications, with a cutoff point of 5 days (less than or equal to or more than 5 days). The entries of hospital stay were also divided into two groups: (1) up to 9 days (normal) and (2) more than 9 days (prolonged).

As the age of 65 years reflects the official retirement age in most Western societies, and ages beyond this are related to an increased risk of mortality [2, 23], we divided our patients in two groups with a cutoff age of 65. Comorbidity was also classified in groups above and below 2 according to Charlson's comorbidity score. Finally, the patients were assigned to two groups concerning surgery duration, using a cutoff limit of 180 min (first group, 120–180 min; long duration group, more than 180 min).

Statistical analysis was performed to evaluate the first 100 consecutive patients using SPSS v. 13.0. Categorical parameters were compared using the Pearson chi-square test or Fisher's exact test. The associations between hospital stay and total hypotension time or between complications and other confounding parameters were tested using multivariate logistic regression, because factors as the Charlson score or complications were described as qualitative factors. Thus, it was obligatory to define some arbitrary but reasonable cutoff points for the continuous factors. The multivariate logistic regression (binary) was used to ascribe any specific risk every variable could separately contribute to the prolonged hospitalization and to complications, when all variables are examined together. On a univariate basis, the risk ascribed to any variable may be attributable to another, highly associated variable. Thus, all factors such as hypotension, age, duration of surgery, and Charlson's score were simultaneously analyzed together by using logistic regression, first with hospital stay, then with complications, etc., to improve the accuracy of predictions. Associations were expressed as unadjusted and adjusted odds ratio (OR) with 95% confidence intervals (CI). An effect was considered significant at $P < 0.05$ (two-tailed test).

Results

Patient demographics and clinical data are shown in Tables 1 and 2. Duration of the operation was equal to or less than 180 min in 53 of our patients and longer than 180 min in the remaining 47. The mean THT in this first subgroup was 16.4 ± 18.4 min; in the second, it was 33.5 ± 44.6 min. In the first subgroup, the number of patients with THT up to 10 min was 31/53 (58.49%) in the first subgroup and 22/47 (46.8%) in the second. In both these groups, the other patients showed greater hypotension times (47 with THT more than 10 min total). For all our patients, regression analysis of THT as a dependent variable to operation time showed a significant relationship ($P < 0.009$).

Table 1 Demographic and clinical characteristics

Age	62.2 (13.9)[a] years
Sex (F/M)	47/53
Body mass index (BMI)	26.0 (4.6)
Alcohol consumption	35
Smoking	27
Medical history	
Previous anesthesia	52
Undermedication	68
Heart disease other than below	15
Angina pectoris-myocardial infarction	8
Renal disease	3
Pulmonary disease	5
Hypertension	46
Stroke	1
Diabetes (insulin-dependent)	12
New York Heart Association (NYHA) > 2	21
American Society of Anesthesiologists (ASA) > 2	32
Charlson's Comorbidity Score > 2	48
Preoperative systolic blood pressure	142.0 (19.6) mmHg
Preoperative diastolic blood pressure	75.3 (10.0) mmHg

[a] Parentheses denote standard deviation

Thirty-seven of our patients stayed in the hospital for 9 or more days or died. Table 3 displays our findings from multivariate logistic regression specifically for the association of our primary variable (total hypotension time) with hospital stay and presence and duration (in days) of postoperative complication(s) to the patients. As shown, total hypotension time was significantly related to these three parameters. A significantly higher percentage of the patients who experienced hypotension time longer than 10 min showed delayed discharge from hospital (26% vs. 11%; adjusted OR 4.56, $P < 0.001$). The percentage of patients with complications was also significantly higher in the hypotensive patients compared with patients with hypotension time of 10 min or less (38% vs. 23%; adjusted OR 5.10, $P < 0.001$). Finally, significantly more patients from the group with hypotension time more than 10 min showed complications lasting 4 days or more (29% vs. 13%; adjusted OR 4.54, $P < 0.001$; Table 3).

Table 4 shows our findings from multivariate logistic regression for the specific relationship of other variables (age, Carlson Comorbidity Score, duration of surgery) with hospital stay, presence or absence of postoperative complication(s), and their duration in days. As shown in Table 4, surgery duration failed to affect hospital stay but was associated with patients who had all types of complications. Age and comorbidity affected neither the hospital stay nor the complications. Sixty-one of our patients developed complication(s) postoperatively, and the summation of their duration was equal or greater than 5 days per patient in 42 patients. The total number of complications was 80 (30 in the group of THT ≤10 min and 50 in the THT >10 min); that is, a patient could suffer from more than one complication during hospitalization (Table 5). Finally, 53 of these complications were serious (36 in the group of THT >10 min vs. 17 in the other group) in terms of affecting major organs such as heart, lungs, and intestines and thus extending patient hospital stay.

Table 2 Intraoperative and postoperative data

Surgery duration	194.5 (70.6)[a] min
Ropivacaine consumption (during surgery)	36.6 (26.5) mg
Hypotension time	24.4 (34.3) min
Transfusion of packed red cells	0.53 (0.858) units
Hospital stay	11.2 (9.5) days
Postoperative epidural analgesia	2.74 (0.97) days
Sleep disturbances	39
Nausea	0.9 (1.9) days
Vomiting	0.3 (1.2) days
Immobilization	1.2 (1.6) days
Immobilized in bed or sitting	1.8 (2.3) days
Fasting	2.0 (2.3) days
Oral liquids	1.7 (1.5) days
Parenteral nutrition	1.4 (3.6) days
Pulmonary complications	21
Cardiovascular complications	12
Gastrointestinal tract complications	25
Wound complications	12
Other type of complications	10
Intensive care unit (postoperatively)	1
Death	1

[a] Parentheses denote standard deviation

Discussion

This is an observational study characterizing the influence of some factors considered significant for postoperative outcomes and especially for "hospitalization" in patients undergoing routine, moderate-risk, elective surgery. The period of observation was limited to the end of hospital stay, and we avoided including every possible factor for hospital time or complications as the risk for spurious findings is greatly increased [24]. We rather chose factors that could be of prior interest such as age, comorbidity,

Table 3 Co-relation between intraoperative hypotension and mobidity/hospital stay

	Total hypotension time (min)		P value	Adjusted odds ratio (OR)	95% confidence interval (CI)
	≤10 (%)	>10 (%)			
Hospital stay (days)					
≤9	42	21	0.001	4.56	1.85–10.96
>9	11	26			
Complications					
No	30	9	0.001	5.10	1.95–13.35
Yes	23	38			
Duration of complications (days)					
Up to 4	40	18	0.001	4.54	1.88–10.92
≥5	13	29			

Table 4 Co-relation between age, Carlson score, duration of surgery and hospital stay, morbidity

	Age (years)		Carlson Comorbidity Score		Duration of surgery (min)	
	≤65	>65 (%)	≤2	>2 (%)	≤180	>180 (%)
Hospital stay (days)						
≤9	34%	29	35%	28	35%	28
>9	16%	21	17%	20	18%	19
P value	0.742		0.689		0.787	
Adjusted OR	1.18		1.22		1.12	
95% CI	0.44–3.16		0.45–3.26		0.47–2.71	
Complications						
No	25%	14	26%	13	27%	12
Yes	25%	36	26%	35	26%	35
P value	0.324		0.148		0.019	
Adjusted OR	1.69		2.17		3.10	
95% CI	0.59–4.81		0.76–6.23		1.20–8.00	
Duration of complications (days)						
Up to 4	33%	25	34%	24	35%	23
≥5	17%	25	18%	24	18%	24
P value	0.5		0.406		0.161	
Adjusted OR	1.40		1.51		1.87	
95% CI	0.52–3.77		0.56–4.07		0.77–4.49	

Table 5 Total complications (80) that occurred in 61 patients and their relationship to time of hypotension

Complications	Hypotension time ≤10 min	Hypotension time >10 min	Summation
Pulmonary	9 (3)	12 (6)	21 (9)
Cardiovascular	4 (1)	8 (7)	12 (8)
Wound infection or healing delay	3 (1)	9 (3)	12 (4)
Gastrointestinal tract			
Ileus			
Paralytic	4 (4)	8 (8)	12 (12)
Mechanical	1 (1)	1 (1)	2 (2)
Dehiscence-inflammation	3 (3)	6 (6)	9 (9)
Hemorrhage	2 (2)	0	2 (2)
Renal	1 (1)	3 (3)	4 (4)
Other			
As persistent fever, etc.	3 (1)	3 (2)	6 (3)

Numbers in parentheses show complications (total, 53) that occurred in patients whose hospital stay was prolonged

surgery duration, and hypotension. Concerning complications, we did not limit our scope only to those severe and life threatening but also included minor forms of morbidity that increase length of hospital stay and healthcare costs. The chosen method for comorbidity validation (Charlson's comorbidity score) has been proved to be superior to previously reported methods such as ASA physical status classification; a Charlson's score of greater than 2 incurred a 16-fold-increased risk of 1-year mortality and, therefore, it is considered a better predictor [2].

Hypotension is common and is more prevalent in situations such as induction of anesthesia [21], use of anesthetic drugs or neuraxial blockade, severe blood loss, or surgical manipulations (e.g., compression of the vena cava). Hypotension is attributable to a number of interacting factors, and, in many instances, it is impossible to define which factor and how it contributes to hypotension during surgery [22]. It is reasonable to assume that the more extensive the surgery is, the more time a patient is likely to be exposed to hypotension. If, therefore, hypotension and duration are risk factors for the patient's outcome, this would be obvious in major abdominal surgery of long duration, a situation where continuous anesthetic and surgical manipulation of the patient exist. The model of elective major intraabdominal operations incorporates all the aforementioned features for evaluation. In agreement with others [25], our study showed that surgery duration, along with hypotension, is a parameter that is strongly associated ($P = 0.019$; Table 4) to all types of complications. Each of these factors contributes by itself to the dependent factor "complication," increasing accordingly the relative risk. Nevertheless, prolonged time of operation in our study does not appear to be associated with prolongation of hospital stay (Table 3), probably because surgery duration fails to associate with complications that exceed the 4-day time period (Table 5) and consequently with prolonged hospitalization.

The correlation between increasing ASA physical status and the risk of postoperative mortality was reported almost four decades ago [26], and physical status and age are still considered factors associated (association, not causation) with increased morbidity and mortality [2, 23, 25]. We chose to include these factors in our search along with hypotension to also check if hypotension contributes to risk not as a single factor but in the presence of these two associated factors. Our results suggest that other factors, as hypotension and hypoperfusion, may hide behind these generally accepted risk factors. Methodological reasons also might be responsible for not finding in our series a clearly positive influence of age and comorbidity on perioperative risk. Our study has several limitations, as happens with any prospective observational study, as it is an inherent weakness of most such studies that the sample may not be representative of the population [24]. However, there was no other preselection except for the exclusion criteria mentioned in Methods. Perhaps the size of the study population was too small to detect such differences. We also must emphasize that to maintain sample homogeneity all operations were elective, abdominal, long-duration procedures and that the anesthetic and surgical teams remained the same throughout the study.

As age and comorbidity are essentially nonmodifiable, we, as do others [25], consider that very little can be done to alter these preoperative variables so as to alter outcome. Consequently, these risk factors can only define, in our study, the role of hypotension relative to complications and to subsequent prolonged hospitalization. Table 5 shows that high in the list of complications prolonging hospital stay are complications of gastrointestinal dysfunction (ileus, trauma dehiscence), as well as pulmonary or cardiac complications, in all types of laparotomic surgery that were performed in this study (general as pancreatic, colon surgery, and partial hepatectomy, or urological as radical prostatectomy, total cystectomy, and nephrectomy). Although all these operations were abdominal, patients who had noticeable hypotension intraoperatively experienced more serious complications of all kinds (intestine, heart, etc.) and failed to leave hospital on time. In turn, intraoperative hypotension may affect all types of complications, especially of heart or lungs (cardiopulmonary complications) or intestines, which is less frequently mentioned in modern literature and needs to be clarified. The last finding is consistent with those of previous studies suggesting that the gastrointestinal tract is extremely sensitive to hypoperfusion, catecholamines, and other insults [27, 28]. In this type of procedure the incidence of postoperative gastrointestinal dysfunction is great, thus confirming the notion that mechanical trauma is a major complication factor. However, trauma cannot be the only cause of dysfunction; in another study [25], 32% of patients with prolonged hospitalization exhibited gastrointestinal dysfunction after extraabdominal operations (e.g., revision hip arthroplasty). Also of note is that cardiac morbidity, in our study, is not the most relevant type of morbidity, as in other studies, after noncardiac surgery [12–15]. In our opinion, this could be true because in these studies, the patient population or the surgery performed were specialized. In contrast, our study enrolled a diverse group of patients undergoing various procedures, which is a likely explanation for the observed differences. In studies reporting a high incidence of cardiac complications, the patients possibly were not rigorously assessed for noncardiac morbidity and this information was not reported. In our study, intestinal complications were not as severe as those of the heart (life threatening) because almost all our cases of paralytic ileus were gradually resolved, leading only to delayed patient discharge. Last, all the foregoing complications, concerning almost every major organ, were strongly associated with hypotension ($P = 0.001$), and the risk for the patients who had more than 10 min total intraoperative hypotension was 4.5 times greater than those who experienced less or no hypotension.

In most of the cases, hypotension indicates tissue hypoperfusion and subsequent inflammation. The stress response to surgery is extremely complex, with both beneficial (improved wound healing and tissue repair) and detrimental (procoagulant and immunosuppressive) effects [11, 28, 29], which are thus implicated in the development of postoperative morbidity. Neuronal responses are activated through nociceptive pathways, and inflammation is associated with the production of cytokines, prostanoids, complement, and other inflammatory factors that act locally to facilitate host defense and repair. Cytokines play a major role in the inflammatory response syndrome after trauma, ischemia–reperfusion injury, and infection, especially sepsis [27, 30]. Anesthetic techniques, surgical factors, and hemodynamic variables such as hypotension are strongly interacting elements and presumably alter the cytokine profile [31, 32]. Blocking the afferent neural stimulus by use of continuous epidural analgesia (a method we used on this particular population) seems to be very effective in reducing the classic catabolic response to an operation, whereas effective pain relief neither affects immune function and inflammation markers [33–35] nor reduces hospital stay [36]. Presently, not a single intervention has been shown to eliminate undesirable operational sequelae by itself; thus, multimodal approaches have been engaged to accelerate recovery and reduce complications and hospital stay [37, 38]. Taking into account all the foregoing, we suggest that hypotension and subsequent hypoperfusion cause dysfunction distally and not directly related to the site of the initial injury organs, especially in such sensitive organs as the heart or gastrointestinal tract [39]. Complications from the heart are well established in the literature, and our suggestion concerning the gastrointestinal tract is consistent with numerous studies that have demonstrated this kind of association in the intensive care unit (ICU) environment [40–42] between organ hypoperfusion, organ dysfunction (complications), and prolonged hospitalization.

In conclusion, these results suggest that intraoperative hypotension is a significant risk factor for postoperative complications. Subsequent hypoperfusion leads to various kinds of complications, especially from sensitive organs, depending on adequate blood flow. Intraoperative hypotension may affect outcomes and alter patient prognosis in more complicated ways than previously appreciated. Anesthetic management intended to avoid hypotension in major abdominal surgeries, as much as possible, may positively affect outcomes, although nowadays it is still very difficult to clearly foresee all the points at which a patient could have hypotension during surgery. Further studies are needed, not only to clarify such a relationship but also to determine treatment that will improve patient outcome.

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