ORIGINAL RESEARCH

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Determining the Factors Affecting the Development of Perioperative Complications According to Aging Stages

Yaşlılık Evrelerine Göre Perioperatif Komplikasyon Gelişimine Etki Eden Faktörlerin Belirlenmesi

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Abstract

Objective: This study aimed to examine perioperative complication risks in elderly patients stratified by age.

Method: Elderly patients (youngest-old, ages 65 to 74 years; middle-old, 75 to 84 years; and oldest-old, ≥85 years) and controls (20-30 years) who underwent surgical intervention under general anesthesia were included in this prospective observational study.

Results: Two-hundred-sixty patients were included. Different age subgroups showed a different course in terms of perioperative complications. For any combined end-point of any perioperative complication, having a body mass index>28 [odds ratio (OR): 2.4; 95% confidence interval (CI): 1.2-4.6; p=0.012] and being on multi-pharmacy regimen at baseline (OR: 1.9; 95% CI: 1.1-3.5; p=0.029) emerged as significant independent predictors. In reference to controls, each elderly age group emerged as a significant independent predictor: youngest-olds (OR: 4.9; 95% CI: 2.2-10.8; p<0.001); middle-olds (OR: 2.5; 95% CI: 1.1-5.4; p=0.025); oldest-olds, (OR: 5.6; 95% CI: 2.5-12.6; p<0.001).

Conclusion: Elderly patients appear to have higher risk for intraoperative and postoperative complications when compared to the young patients, and each age group appears to have increased risk for different type of complications.

Keywords: Complications, elderly, middle-old, surgery, oldest-old, youngest-old

Öz

Amaç: Bu çalışma yaşa göre katmanlara ayrılmış yaşlı hastalarda perioperatif komplikasyon risklerini incelemeyi amaçlamıştır.

Yöntem: Bu prospektif gözlemsel çalışmaya, genel anestezi altında cerrahi girişim yapılan yaşlı hastalar (yaşlı hastalar, 65-74 yaş; ileri yaşlı hastalar, 75-84 yaş; ve çok ileri yaşlı hastalar, ≥85 yaş) ve kontrol grubu (20-30 yaş) dahil edilmiştir.

Bulgular: İki yüz altmış hasta çalışmaya dahil edilmiştir. Farklı yaş alt grupları perioperatif komplikasyonlar açısından farklı seyir göstermiştir. Herhangi bir komplikasyon olması şeklindeki kombine sonlanım noktası için, vücut kitle indeksi>28 olması [olasılık oranı (OO): 2,4; %95 güven aralığı (GA): 1,2-4,6; p=0,012] ve başlangıçta çoklu ilaç kullanıyor olmak (OO: 1,9; %95 GA: 1,1-3,5; p=0,029) anlamlı bağımsız belirleyiciler olarak bulunmuştur. Kontrollere göre, her bir yaşlı alt grubunda bulunmak anlamlı bağımsız belirleyici olarak saptanmıştır: Yaşlılar (OO: 4,9; %95 GA: 2,2-10,8; p<0,001); ileri yaşlılar (OO: 2,5; %95 GA: 1,1-5,4; p=0,025); çok ileri yaşlılar (OO: 5,6; %95 GA: 2,5-12,6; p<0,001).

Sonuç: Genç hastalarla karşılaştırıldığında, yaşlı hastalar intraoperatif ve postoperatif komplikasyonlar açısından yüksek risk altında görünmektedir ve her bir yaş grubunun farklı tip komplikasyonlar için riski artmıştır.

Anahtar kelimeler: Cerrahi, çok ileri yaşlı, ileri yaşlı, komplikasyonlar, yaşlı, yaşlılar

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Introduction

World population is becoming gradually older (1), and proportion of elderly people is expected to double by 2050 (2). Advanced medical technologies and better healthcare facilities together with improved living conditions seem to be the main causes of such increase. Population aging is associated with increases in the prevalence of chronic diseases and complex medical conditions; therefore, healthcare systems need to respond and adapt such demands for specialized care (1).

Owing to the overall aging of the population, gradually more elderly become candidates for surgical interventions (3,4). Older individuals more frequently utilize healthcare facilities, and they have higher rates for inpatient and outpatient surgical and non-surgical procedures (5-8). In England, people who underwent surgery almost doubled between the years of 2004 and 2007 and the years of 2014 and 2015, and nearly one-third of these patients are older than 85 years (9).

Old age is commonly considered a risk factor for anesthesia and surgery and has been included as a scoring item in most known risk stratification tools (10,11), although frailty rather than chronological age may also be considered to estimate risks associated with cumulative age-related decline in physiological systems (9,12,13). In general, elderly require higher level of perioperative care when compared to the younger patients since they are prone to develop postoperative complications, functional impairment, and dependency (3).

To date, several studies have examined the complication rates in different old age groups, but with particular emphasis on postoperative complications (14-18). Due to structural and functional deterioration of physiological systems, elderly is not only prone to postoperative surgical complications, but also intraoperative problems as well. Identifying age-related perioperative risks before a surgical intervention would aid to provide better intraoperative management and postoperative care; thus, would improve surgical outcomes and consequent healthcare costs.

This study aimed to examine the intraoperative as well as postoperative risks in elderly patients stratified by age (youngest-old, middle-old, oldest-old), in comparison with young adults.

Materials and Methods

Patients

Elderly patients and controls who underwent surgical intervention under general anesthesia were included in this prospective observational study. Three groups of elderly patients stratified for age (youngest-old, ages 65 to 74 years; middle-old, 75 to 84 years; and oldest-old, ≥85 years) and young controls (20 to 30 years old) comprised the study groups. Sixty-five consecutive eligible patients were included into each group. Patients who underwent a surgical intervention shorter than two hours were excluded. The study protocol was approved by the Local Ethics Committee (Marmara University Medical Faculty Ethics Committee for Clinical Research, no: 09.2016.438; date: 15.07.2016) and the study was conducted in accordance with the Declaration of Helsinki.

Anesthesia Management

Anesthesia was induced by 1.5-2 mg/kg propofol and 0.6 mg/kg rocuronium and maintained by desflurane or sevoflurane, depending on the decision of the anesthesiologist. The dose of inhalational anesthetic was adjusted to keep bispectral index between 35 and 45.

Perioperative Assessments

Besides body mass index (BMI), operation type and number of medications were recorded for each patient. Intraoperatively, heart rate (HR), mean arterial pressure (MAP), body temperature (TEMP), bispectral index (BIS), and train of four (TOF) were continuously monitored throughout the operation and were recorded every 30 minutes. HR and MAP were measured non-invasively. Body temperature was measured using forehead skin probe. Depth of anesthesia was monitored using BIS (Aspect Medical Systems, Natick, Mass, ABD). Train of four measurements were done using a muscle-nerve stimulator. Two electrodes were placed over the region innervated by the ulnar nerve in the arm just above the wrist (negative electrode distally, positive electrode proximally). Movement sensor and temperature probe were placed on the thumb and hypothenar region of the hand, respectively. A 2 Hz stimulation was administered every 0.5 seconds. Basal train-of-four value provided by the device was recorded and this value was monitored throughout the operation; in addition, this value aided in the intubation and extubation of the patient.

In addition, duration of anesthesia/surgery and intraoperative complications as well as ephedrine, atropine,

norepinephrine, and glyceryl trinitrate use were recorded. Postoperatively, post-anesthesia care unit (PACU) stay time, delayed awakening, intensive care unit (ICU) admission, nausea/vomiting, and postoperative complications were recorded. Patients were asked to self-evaluate their pain using 10-point visual analogue scale (VAS) (0, no pain; 10, worst imaginable pain) at the time of awakening. In addition, the groups were compared for the combined end-point of any perioperative complication or death defined as follows (some are intraoperative untoward events): Atelectasis, bronchospasm, re-intubation, bradycardia, hypotension, desaturation, hypertension, hyperglycemia, hyponatremia, tachycardia, bleeding, laryngospasm, subcutaneous emphysema, or mortality (within 30 days after or during the operation).

Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 21.0 was used for data analysis. Graphical methods and hypothesis tests were used to test the normality of continuous variables. For intergroup comparisons of continuous data, the One-Way ANOVA or Kruskal-Wallis test was employed, where appropriate; and for pairwise comparisons, the Tukey HSD, Games-Howell, or built in post-hoc test of Kruskal-Wallis was used. For intergroup comparisons of categorical data, the Pearson's chi-square test was utilized, and Bonferroni correction was performed for pairwise comparisons of the groups. To compare the groups in terms of changes in intraoperative measurements (HR, MAP, TEMP, BIS, TOP), Two-Way ANOVA for repeated measurements was used and for pairwise comparisons of the groups, LSD test was preferred. Logistic regression was used for multivariate analysis of potential predictors of any perioperative complication. Receiver operating characteristic curves were evaluated to identify optimal cut-off values for continuous variables to be incorporated in multivariate analysis. A p-value <0.05 was considered an indication of statistical significance.

Results

A total of 260 patients equally distributed to four study groups were included in the study. Distribution of surgery types was as follows: General surgery operations (n=134, 51.5%), orthopedic surgery (n=53, 20.4%), eye surgery (n=36, 13.8%), and others (n=37, 14.2%) (neurosurgery, plastic and reconstructive surgery, urology, thoracic and cardiovascular surgery, obstetrics surgery). Anesthetic type was desflurane and sevoflurane in 137 (52.7%) and 123 (47.3%) patients, respectively. The study groups did not differ regarding BMI (p=0.206), but number of medications was significantly higher in elderly patient groups when compared to controls (Table 1).

Comparison of Perioperative Parameters

Table 1 shows comparisons of intra- and post-operative characteristics of the four groups. Although differences in duration of anesthesia did not reach statistical significance on pairwise comparisons, duration of surgery was significantly longer in the oldest-old group when compared to the youngest-old group. The groups did not differ regarding atropine and nitroglycerine need; however, vasopressor (ephedrine, norepinephrine) need was higher in all elderly groups when compared to controls.

Delayed awakening was more common among the middle old and oldest-old groups and PACU stay time was longer in all elderly groups. ICU admission was more common among the oldest-old group, when compared to controls only. In contrast, the middle-old and oldest-old groups had lower VAS score when awakening, compared to controls and youngest-olds. None of the groups emerged as significantly different from others in terms of nausea/vomiting and mortality.

Comparison of the Groups in Terms of Perioperative Complications

All three elderly groups [youngest-olds, odds ratio (OR): 5.6 (95% confidence interval (CI): 2.6-12.0, p<0.001; middle-olds, OR: 2.8 [95% CI: 1.3-5.9], p=0.007; oldest-olds, OR: 6.0 [95% CI: 2.8-12.8], p<0.001] had significantly higher perioperative complication rate when compared to controls, without any difference between each elderly group (Table 1).

Predictors of Any Perioperative Complication

On multivariate analysis, age groups, a BMI>28 (OR: 2.4; 95% CI: 1.2-4.6; p=0.012), and being on multi-pharmacy regimen at baseline (OR: 1.9; 95% CI: 1.1-3.5; p=0.029) emerged as significant independent predictors of any perioperative complication. In reference to controls, each elderly age group emerged as a significant independent predictor: youngest-olds (OR: 4.9; 95% CI: 2.2-10.8; p<0.001); middle-olds (OR: 2.5; 95% CI: 1.1-5.4; p=0.025); oldest-olds, (OR: 5.6; 95% CI: 2.5-12.6; p<0.001).

Changes in Intraoperative Parameters Over Time

Figure 1 shows intraoperative changes in HR, MAP, body temperature, BIS, and TOF of the four groups. The groups did not differ in terms of changes in HR (p<0.076); on the other hand, they differed in terms of changes in other

Table 1. Comparison of clinical and perioperative characteristics of the groups

	Youngest-old (65-74 y)	Middle-old (75-84 y)	Oldest-old (≥85 y)	Controls (20-30 y)	p
Clinical characteristics					
BMI, kg/m^2	25.4±3.5	24.9±3.8	23.9±3.8	24.7±4.6	0.206
No. of medications	1.4±1.1†	1.3±1.3†	1.5±1.0†	0.49±0.7	<0.001
Intraoperative parameters					
Duration of anesthesia, min	169.4±49.6	151.2±31.1	158.3±30.2	153.9±38.2	0.043*
Duration of surgery, min	147.4±36.2	131.3±21.5	132.5±30.5‡	138.5±31.9	0.022
Atropine need	4 (6.2%)	6 (9.2%)	7 (10.8%)	2 (3.1%)	0.341
Nitroglycerine need	4 (6.2%)	2 (3.1%)	2 (3.1%)	0 (0.0%)	0.248
Vasopressor need	34 (13.8%)†	27 (52.3%)†	28 (41.5%)†	9 (43.1%)	<0.001
Postoperative characteristics					
Delayed awakening	8 (12.3%)	16 (24.6%)†	25 (38.5%)†,‡	3 (4.6%)	<0.001
PACU stay time, min	19.8±8.1†,‡,§	23.2±7.2†	26.4±8.3†	11.5±2.6	<0.001
Awakening VAS>3	44 (67.7%)	1 (1.5%)†,‡	0 (0.0%)†,‡	42 (64.6%)	<0.001
ICU admission	6 (9.2%)	10 (15.4%)	14 (21.5%)†	2 (3.1%)	0.010
Nausea-vomiting	20 (30.8%)	13 (20.0%)	10 (15.4%)	10 (15.4%)	0.097
Mortality	1 (1.5%)	3 (4.6%)	6 (9.2%)	0 (0.0%)	0.003*
Primary endpoint					
Any complication or mortality†	42 (64.6%)†	31 (47.7%)†	43 (66.2%)†	16 (24.6%)	<0.001

Following were the perioperative untoward events classified as a complication (some are intraoperative untoward events): Atelectasis, bronchospasm, re-intubation, bradycardia, hypotension, desaturation, hypertension, hyperglycemia, hyponatremia, tachycardia, bleeding, laryngospasm, subcutaneous emphysema, or mortality (within 30 days after or during the operation).

†: Significantly different than controls, ‡: Significantly different than the youngest-old group, §: Significantly different than the middle-old group, *: Pairwise comparisons with correction did not reveal any significant difference between the groups, VAS: Visual analogue scale, BMI: Body mass index, PACU: Post-anesthesia care unit, ICU: Intensive care unit

parameters (p=0.002, p<0.001, p<0.001, and p<0.001, for MAP, TEMP, BIS, and TOR, respectively).

Pairwise comparisons revealed overall mean differences between groups regarding the course throughout the operation. Overall, in controls, MAP was significantly lower than in the youngest-old and middle-old groups (p=0.003 and p=0.033, respectively), but higher than in the oldest-old group (p=0.018). The oldest-old group had significantly lower MAP when compared to the youngest-old and middle-old groups (p<0.001 for both). Body temperature was the highest among controls and significantly and gradually decreased by increasing age (p<0.005 for all comparisons). Although anesthesia depth was adjusted using BIS scores, the youngest-old group had the highest BIS scores (p<0.05 for all), and the oldest-old group had the lowest BIS scores when compared to other groups (p<0.05 for all) throughout the operation. Controls had the lowest TOF scores when compared to all other groups (p<0.01 for all), and the middle-old and oldest old groups had the highest TOF scores (p<0.05 for all); however, no difference was evident between the two latter groups (p=0.158).

Discussion

Findings of this study suggest that there may be unique perioperative course characteristics for individual elderly patient groups. Increased vasopressor need, longer PACU stay time, higher postoperative complication rate, and low body temperature were evident for all elderly patient groups. Delayed awakening, higher intraoperative blood pressure, and higher TOF scores were the issues seen in the youngest-old and middle-old groups. Increased pain on awakening and higher BIS scores seem to be concerns for youngest-olds, whereas surgery time was longer in oldest-olds. Although several studies have so far tested postoperative complication rates among individual age groups of elderly patients, the present study not only focuses on postoperative course, but also on intraoperative and immediately postoperative course.

This study found higher complication rates in all elderly groups when compared to younger patients (<65 years). This is in line with previous observations indicating that age is a risk factor for surgical complications and other unwanted events, even after adjustment for preoperative

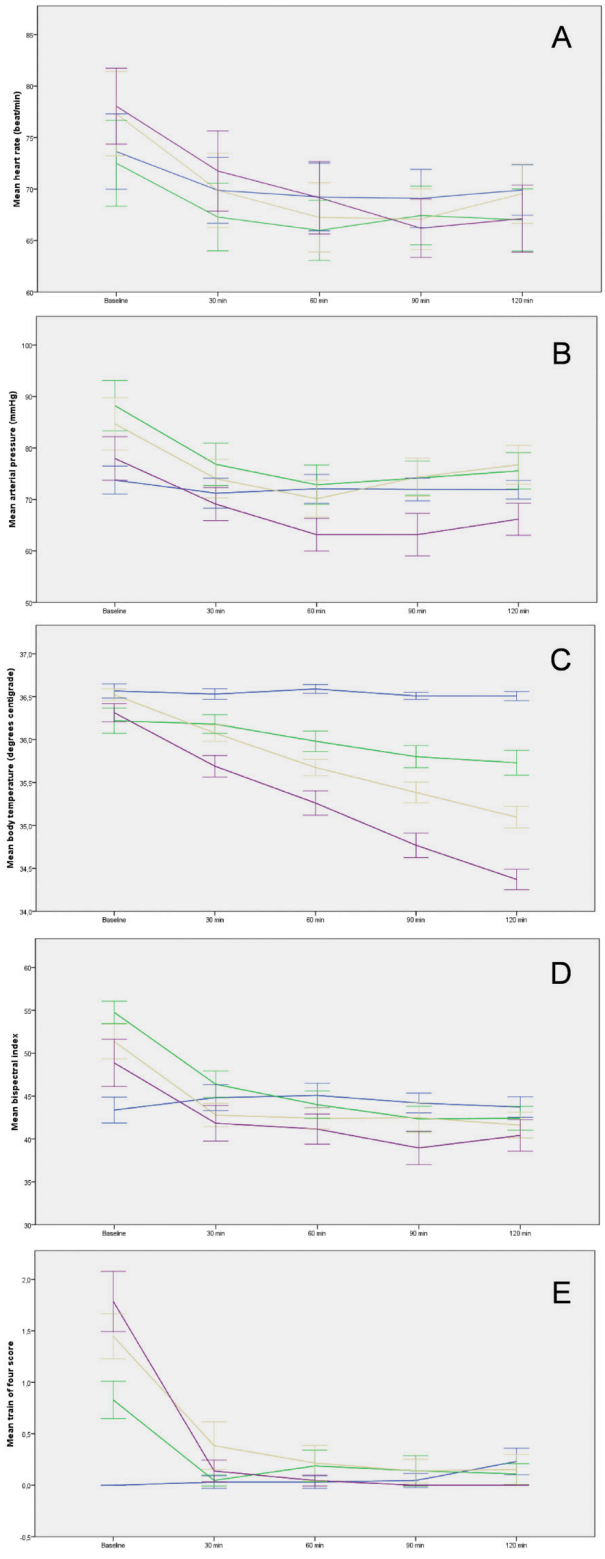


Figure 1. Changes in mean heart rate (A), arterial pressure (B), body temperature (C), bispectral index (D), and train of four score (E) over time during the operation. Error bars indicate 95% confidence intervals. Line colors for each group: Controls (20-30 y), blue; youngest-old group (65-74 y), green; middle-old group (75-84 y), gray; oldest-old group (≥85 y) violet

co-morbidities (19-21). Age has been found to be an independent predictor for postoperative complications after rectal and colon cancer (21).

To date, several studies have compared different elderly age sub-groups mainly in terms of postoperative complications. A 2014 study compared postoperative complication rates in two elderly groups, which correspond to middle-old and oldest-old patients in the present study, who underwent radical cystectomy (14). In line with our findings, that study did not find any difference between the two groups in terms of any complication rate as well as duration of hospital stay, major complication rate or 3-year survival, although 90-day mortality was higher in the oldest-old group. However, it is of note to mention that the study focused on postoperative complications. The present study, on the other hand, also included intraoperative complications into the analysis.

A recent study compared three different elderly patient groups and young patients who underwent percutaneous nephrolithotomy in terms of surgical outcomes and complications (15). Age stratification was slightly different than the present study: Young patients (18-64 years), 65-69 years, 70-79 years, and 80+ years. No significant difference was found between young patients and elderly patients (≥65 years) in terms of duration of hospitalization, duration of hospitalization, blood transfusion, any complication, major complication, or urinary tract infection rates. In addition, elderly subgroups did not differ in terms of these parameters.

Another study examining the predictors of postoperative complications in two elderly patient groups (75-84 and ≥85 years) who underwent surgery for gastric cancer did not find any difference in terms of postoperative complications (16).

A recent Japanese study compared complication rates in younger adults and three age groups of elderly patients after spine surgery for spinal stenosis. In that study, an increase in total and medical complications were evident with increasing age; however, such a relationship was not found for surgical complications (17).

On the other hand, a study including a large series of cases (more than 25.000 women) who underwent surgery for endometrial cancer found differences between old age groups in terms of complications (18). In that study, where five different elderly age groups were examined, women at their sixties were more likely to have perioperative surgical complications as well as postoperative medical complications when compared to oldest olds (≥85 years).

In addition, relatively younger old age was associated with longer hospital stay, more frequent transfusion requirement, and increased mortality. Increased morbidity of older age persisted even after adjustment for medical co-morbidities.

Relatively few studies examining the effect of elderly age group on surgical complications mainly focused on postoperative complications. However, the present study also included intraoperative complication into the analyses, considering that elderly people would be rather fragile under general anesthesia and period of surgery would also pose risks for that particular age group.

An important implication of our findings is the predominance of particular complications in each elderly age group. Although subgroups of elderly were not different in terms of the combined endpoint (any complication), several complication types appeared to be unique for particular age groups. Therefore, we believe that each elderly patient should be considered individually for operative risks through the evaluation of the functional status of the organ systems as well as by taking into account the particular age subgroup of the patient.

Study Limitations

Lack of any cognitive evaluation may be considered as a limitation of the present study since any cognitive impairment after surgery would be regarded as a surgical complication.

Conclusion

The elderly patients appear to have higher risk for perioperative and postoperative complications when compared to the young patients. However, although individual elderly age groups do not differ in terms of overall complication rate, each group appears to have increased risk for different type of complications. Larger studies are warranted to shed light on the individual age related perioperative and postoperative risks for the elderly patients.

Ethics

Ethics Committee Approval: The study protocol was approved by the Local Ethics Committee (Marmara University Medical Faculty Ethics Committee for Clinical Research, no: 09.2016.438; date: 15.07.2016) and the study was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Elderly patients and controls who underwent surgical intervention under general anesthesia were included in this prospective observational study. Three groups of elderly patients stratified for age (youngest-old, ages 65 to 74 years; middle-old, 75 to 84 years; and oldest-old, ≥85 years) and young controls (20 to 30 years old) comprised the study groups. Sixty-five consecutive eligible patients were included into each group. Patients who underwent a surgical intervention shorter than two hours were excluded.

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Authorship Contributions

Surgical and Medical Practices: M.O.E., S.Ü.Z., P.Ç.D., Concept: M.O.E., S.Ü.Z., Design: M.O.E., Data Collection or Processing: M.O.E., Analysis or Interpretation: M.O.E., S.Ü.Z., P.Ç.D., T.U., Z.A., Literature Search: M.O.E., P.Ç.D., T.U., Z.A., Writing: M.O.E., S.Ü.Z.

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