

Impact of total intravenous anesthesia compared with inhalation anesthesia on mortality in oncologic surgery: A retrospective cohort

Dory M. Fernandez-Delgado

Clínica Oncosalud

Cielo A. Estela-Fernandez

estelacielo81@gmail.com

Universidad Científica del Sur

Sebastian Y. Montesinos

Universidad Científica del Sur

Yerson Alberca-Naira

Universidad Científica del Sur

Fernando M. Runzer-Colmenares

Universidad Científica del Sur

Cristina Quiroz-Narvaez

Universidad Científica del Sur

Betzy C. Torres-Zegarra

Universidad Científica del Sur

Nallely V. Chapoñan-Agip

Universidad Científica del Sur

Mayra C. Valenzuela Segovia

Universidad Científica del Sur

Iván C. Aguilar-Marín

Universidad Científica del Sur

César F. Gálvez-Bustamante

Universidad Científica del Sur

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Abstract

Background

Cancer is one of the most important fields of research and affects public health worldwide, with approximately 9.6 million deaths annually. Surgical resection remains the first-line treatment for most malignant solid tumors; however, metastasis and recurrence after surgery persist and are the leading causes of death in cancer patients. In recent years, considerable attention has been paid to the type of anesthesia administered during surgery. The aim of this study is to evaluate the mortality rate among cancer patients receiving IA and those receiving TIVA in a private clinic in Peru.

Methods

A retrospective cohort study was conducted. A total of 1008 cancer patients who underwent resection surgery at a private clinic in Peru between 2014 and 2020 were included. The study design and presentation were based on the guidelines established by the STROBE guidelines. Multivariate analysis using adjusted Poisson regression was performed to estimate relative risks, controlling for age, sex, tumor recurrence, ASA physical status, cancer type, histological grade, type of surgery, transfusions, complications, adjuvant treatments, and comorbidity.

Results

Survival analysis using Kaplan–Meier curves showed no statistically significant differences in overall survival between TIVA and IA. Multivariate analysis using adjusted Poisson regression showed that IA was associated with higher mortality compared to TIVA. (RR: 1.32; 95% CI: 1.01–1.70; $P = 0.038$), regardless of clinical and sociodemographic factors, including tumor recurrence, age, physical status, cancer type, histological grade, type of surgery, transfusions, complications, adjuvant treatments, and comorbidity.

Conclusion

Although the results suggest a possible benefit of TIVA over IA in terms of mortality, these findings should be interpreted with caution.

Background

Cancer is undoubtedly one of the most prominent areas of research and affects public health worldwide, with approximately 9.6 million deaths annually (1, 2). According to the GLOBOCAN 2020 report, this figure is expected to rise to 28.4 million new cancer cases each year by 2040 (3). The first line of

treatment for most malignant solid tumors is surgical resection; however, metastasis and recurrence after surgery persist and are the leading causes of death in cancer patients (4, 5).

Many different factors determine the type of recurrence, severity, and incidence, including cancer malignancy, trauma, surgical stress, adjuvant therapies, and surgical technique, among others (6). In recent years, considerable attention has been paid to the type of anesthesia administered during surgery, as it can alter the balance of host immune surveillance and tumor aggressiveness, both of which are linked to cancer recurrence and spread (7–9).

The most commonly studied anesthetics are inhalation anesthesia (IA), which modulates both the innate and adaptive immune systems, and total intravenous anesthesia (TIVA), which has an anti-inflammatory effect and promotes immune system activity (4, 10–12). Despite growing evidence suggesting that TIVA could offer benefits in terms of oncological outcomes, controversy remains in the current literature (13–16). Previous studies have been predominantly conducted in various contexts and have not specifically addressed Latin American populations, such as those in Peru. The main objective of this study is to evaluate the mortality rate among cancer patients receiving IA and those receiving TIVA in a private clinic in Peru.

Study Design and Methods

A retrospective cohort study was conducted. A total of 1008 cancer patients who underwent resection surgery at a private clinic in Peru between 2014 and 2020 were included. The study design and presentation were based on the guidelines established by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (17).

The study included patients aged 18 years or older who underwent resection surgery for different types of cancer, such as breast cancer, colorectal cancer, and others (**see** Table 1). Patients who received IA or TIVA during surgery were included. Those with incomplete electronic medical records, emergency surgery, minor surgery requiring only local anesthesia, and exploratory surgery were excluded from the study. The variables analyzed included: postoperative mortality, type of anesthesia, age, sex, body mass index, American Society of Anesthesiologists (ASA) physical status, risk behaviours, and Charlson Comorbidity Index (CCI).

Table 1
Baseline characteristics of patients according to type of anesthesia

	Type of anesthesia		P value
	TIVA (n = 429)	IA (n = 579)	
	Mean (years) ± SD		0.010
Age	60.9 ± 13.8	58.6 ± 14.4	
	n (%)		
Sex			
Male	147 (34.4)	177 (30.6)	
Female	281 (65.7)	402 (69.4)	0.205
Risk behaviors			
None	335 (78.1)	460 (79.5)	
One	67 (15.6)	90 (15.5)	
Two or more	27 (6.3)	29 (5.0)	0.673
ASA			
I	23 (5.4)	42 (7.4)	
II	387 (90.2)	495 (87.0)	
III	19 (4.4)	32 (5.6)	0.286
Cancer Type			
Urogenital	86 (20.1)	144 (24.9)	
Gynecological	49 (11.4)	57 (9.8)	
Breast	101 (23.5)	202 (34.9)	
Gastrointestinal	123 (28.7)	91 (15.7)	
Thyroid	58 (13.5)	78 (13.5)	
Lung	12 (2.8)	7 (1.2)	< 0.001
Degree of histological differentiation			
Well differentiated	75 (17.6)	151 (26.5)	
*For age: Difference in means: 2.32 (95% CI: 0.5 to 4.1)			
*CCI: Charlson Comorbidity Index. ASA: ASA Physical Status Classification System. TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.			

	Type of anesthesia		P value
	TIVA (n = 429)	IA (n = 579)	
Moderately differentiated	257 (60.3)	254 (44.6)	< 0.001
Poorly differentiated	94 (22.1)	165 (29.0)	
Type of surgery			
Laparoscopic	99 (23.1)	126 (21.8)	0.606
Open	329 (76.9)	453 (78.2)	
Transfusion			
Yes	46 (10.7)	105 (18.1)	< 0.001
No	383 (89.3)	474 (81.9)	
Complications			
Yes	68 (15.9)	35 (6.0)	< 0.001
No	361 (84.2)	544 (94.0)	
Chemotherapy			
Yes	162 (37.9)	220 (38.1)	0.945
No	266 (62.2)	358 (61.9)	
Radiotherapy			
Yes	118 (27.6)	201 (34.8)	0.015
No	310 (72.4)	377 (65.2)	
CCI			
Low comorbidity	338 (78.8)	432 (74.6)	0.123
High comorbidity	91 (21.2)	147 (25.4)	
Recurrence			
Yes	99 (23.1)	99 (17.1)	0.018
No	330 (76.9)	480 (82.9)	
Mortality			
*For age: Difference in means: 2.32 (95% CI: 0.5 to 4.1)			
*CCI: Charlson Comorbidity Index. ASA: ASA Physical Status Classification System. TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.			

	Type of anesthesia		P value
	TIVA (n = 429)	IA (n = 579)	
Yes	68 (15.9)	92 (15.9)	0.987
No	361 (84.2)	487 (84.1)	
*For age: Difference in means: 2.32 (95% CI: 0.5 to 4.1)			
*CCI: Charlson Comorbidity Index. ASA: ASA Physical Status Classification System. TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.			

Table 1

S. Association between type of anesthesia and risk of mortality in cancer patients (adjusted Cox regression model)

Type of anesthesia	HR (IC 95%)	valor P
TIVA (ref.)	—	—
IA	0.88 (0.60–1.30)	0.530
*The Cox regression model was adjusted for multiple potentially confounding clinical and sociodemographic variables, including: tumor recurrence, age, sex, risk behaviors, ASA classification, cancer type, tumor differentiation grade, type of surgery, duration of surgery, transfusions, hospital stay, postoperative complications, chemotherapy and radiotherapy treatment, as well as the Charlson comorbidity index.		
*TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.		

Statistics

Bivariate regression models were used to assess the impact of anesthesia type on mortality, while controlling for relevant covariates, including age, sex, type of cancer, and comorbidities. The chi-square test was used to determine differences between groups for categorical data, and a student's t-test was used for continuous variables. A subgroup analysis of mortality by clinical stage and type of anesthesia was also conducted. Poisson regression was then performed to see the association between type of anesthesia and hospital mortality. In addition, mortality was analyzed using Kaplan-Meier estimation and log-rank analysis to compare mortality rates between groups of patients who received IA and those who received TIVA. Analyses were conducted using available data for each variable. Participants with missing data were included in analyses for which the relevant variables were available. The analysis was performed with STATA version 17.

Results

A total of 1008 patients were included, of whom 429 received TIVA and 579 received IA. Patients in the TIVA group were slightly older than those in the IA group (60.9 ± 13.8 vs. 58.6 ± 14.4 years; $P = 0.010$).

Overall mortality was 15.9%, with no differences between TIVA and IA (15.9% in both groups; $P = 0.987$). Tumor recurrence was more frequent in TIVA than in IA (23.1% vs. 17.1%; $P = 0.018$). Table 1 summarizes the baseline characteristics of patients according to the type of anesthesia. On average, participants had a follow-up of 2317.6 ± 1001.9 days, an anesthetic duration of 147.2 ± 76.5 minutes, and a hospital stay of 4.7 ± 4.0 days.

As shown in Table 2, mortality was associated with older age (63.6 ± 14.2 vs. 58.8 ± 14.1 years; $P < 0.001$), high ASA physical status ($P = 0.042$), gastrointestinal or lung cancer ($P < 0.001$), poor tumor differentiation ($P < 0.001$), open surgery ($P < 0.001$), transfusion ($P < 0.001$), postoperative complications ($P < 0.001$), chemotherapy and radiotherapy ($P < 0.001$), high comorbidity according to the CCI ($P < 0.001$), and tumor recurrence ($P < 0.001$).

Table 2
Bivariate analysis of baseline characteristics in relation to mortality

	Mortality		valor P
	No (n = 848)	Yes (n = 160)	
	Mean (years) ± SD		
Age	58.8 ± 14.1	63.6 ± 14.2	< 0.001
	n (%)		
Sex			
Male	266 (31.4)	58 (36.3)	
Female	581 (68.6)	102 (63.8)	0.229
Risk behaviors			
None	674 (79.5)	121 (75.6)	
One	127 (15.0)	30 (18.6)	
Two or more	47 (5.5)	9 (5.6)	0.476
ASA			
I	58 (6.9)	7 (4.4)	
II	743 (88.7)	139 (86.9)	
III	37 (4.4)	14 (8.8)	0.042
Cancer Type			
Urogenital	194 (22.9)	36 (22.5)	
Gynecological	77 (9.1)	29 (18.1)	
Breast	262 (30.9)	41 (25.6)	
Gastrointestinal	169 (19.9)	45 (28.1)	
Thyroid	133 (15.7)	3 (1.9)	
Lung	13 (1.5)	6 (3.8)	< 0.001
Degree of histological differentiation			
Well differentiated	212 (25.1)	14 (9.2)	
*For age: Difference in means: -4.8 (95% CI: -7.2 to -2.4)			
*CCI: Charlson Comorbidity Index. ASA: ASA Physical Status Classification System. TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.			

	Mortality		valor P
	No (n = 848)	Yes (n = 160)	
Moderately differentiated	464 (55.0)	47 (30.9)	
Poorly differentiated	168 (19.9)	91 (59.9)	< 0.001
Type of surgery			
Laparoscopic	170 (20.1)	55 (34.4)	
Open	677 (79.9)	105 (65.6)	< 0.001
Transfusion			
Yes	111 (13.1)	40 (25.0)	
No	737 (86.9)	120 (75.0)	< 0.001
Complications			
Yes	70 (8.3)	33 (20.6)	
No	778 (91.8)	127 (79.4)	< 0.001
Chemotherapy			
Yes	269 (31.8)	113 (70.6)	
No	577 (68.2)	47 (29.4)	< 0.001
Radiotherapy			
Yes	250 (29.6)	69 (43.1)	
No	596 (70.5)	91 (56.9)	0.001
CCI			
Low comorbidity	705 (83.1)	65 (40.6)	
High comorbidity	143 (16.9)	95 (59.4)	< 0.001
Recurrence			
Yes	94 (11.1)	104 (65.0)	
No	754 (88.9)	56 (35.0)	< 0.001
Type of anesthesia			
*For age: Difference in means: -4.8 (95% CI: -7.2 to -2.4)			
*CCI: Charlson Comorbidity Index. ASA: ASA Physical Status Classification System. TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.			

	Mortality		valor P
	No (n = 848)	Yes (n = 160)	
TIVA	361 (42.6)	68 (42.5)	< 0.001
IA	487 (57.4)	92 (57.5)	
*For age: Difference in means: -4.8 (95% CI: -7.2 to -2.4)			
*CCI: Charlson Comorbidity Index. ASA: ASA Physical Status Classification System. TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.			

Figure 1 shows how mortality is distributed by clinical stage and type of anesthesia. The bar graph shows mortality rates for patients who received TIVA and those who received IA for early-stage (Stage 0–2) and advanced-stage (Stage 3–4) cancers. In early-stage cancer, mortality was slightly lower with IA than with TIVA. However, for advanced-stage cancer, IA had a higher mortality than TIVA.

Survival analysis using Kaplan–Meier curves (Fig. 2) showed no statistically significant differences in overall survival between TIVA and IA. Although both curves showed parallel trajectories and a gradual decline pattern throughout follow-up, TIVA showed a slight reduction in survival in the later intervals, although this difference was not statistically significant. Multivariate analysis using adjusted Poisson regression (Table 3) showed that IA was associated with higher mortality compared with TIVA (RR: 1.32; 95% CI: 1.01–1.70; P = 0.038), regardless of clinical and sociodemographic factors, including tumor recurrence, age, physical status, cancer type, histological grade, type of surgery, transfusions, complications, adjuvant treatments, and comorbidity.

Table 3
Association between type of anesthesia and risk of mortality in cancer patients (adjusted Poisson regression model)

Type of anesthesia	IRR (IC 95%)	P value
TIVA (ref.)	—	—
IA	1.32 (1.01–1.70)	0.038
*The Poisson regression model was adjusted for multiple potentially confounding clinical and sociodemographic variables, including: Tumor recurrence, age, sex, risk behaviors, ASA classification, cancer type, tumor differentiation grade, type of surgery, duration of surgery, transfusions, hospital stay, postoperative complications, chemotherapy and radiotherapy treatment, as well as the Charlson comorbidity index.		
*TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.		
*TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.		

The supplementary material presents the results of the adjusted Cox regression model (**Table S1**), which showed no significant differences between TIVA and IA (HR: 0.88; 95% CI: 0.60–1.30; P = 0.530).

However, this model was considered exploratory because the proportional hazards assumption required for Cox regression was violated, limiting its validity for this dataset.

Discussion

In this study, we found that IA was associated with a higher risk of mortality compared to TIVA, regardless of clinical and sociodemographic factors. This finding suggests that the choice of anesthetic technique could have a relevant clinical impact on perioperative and postoperative outcomes in cancer patients. However, when applying the Cox regression model, the association was no longer significant. In this context, the Cox model was not the most appropriate for the cohort analyzed, which is why it was not considered as the primary analysis. Nevertheless, it is worth mentioning, as it contributes to a more complete and balanced view of the evidence obtained.

On the other hand, the analysis confirmed the association between mortality and multiple well-recognized prognostic factors, such as older age, high ASA physical status, presence of gastrointestinal and lung cancer, poor tumor differentiation, open surgery, need for blood transfusion, postoperative complications, high comorbidity, and use of adjuvant treatments. These findings are consistent with previous literature. Taken together, these data reinforce the fact that surgical outcomes in cancer patients are the result of multiple clinical and demographic factors that must also be taken into account in the prognosis of cancer patients. Likewise, a particular finding in this cohort was the higher frequency of tumor recurrence in the TIVA group. Although this result appears to contradict the observed benefit in mortality, it is likely due to differences in the distribution of cancer type and histological grade between the groups, rather than to the anesthetic technique itself.

Previous studies have reported advantages of using TIVA on survival in cancer surgery. For example, a meta-analysis showed that the TIVA group had a higher overall survival rate (HR = 0.49, 95% CI: 0.30–0.80) (18). Similarly, another study found that TIVA is associated with better overall survival in patients with lung, gastric, colorectal, and pancreatic cancer (19). However, some studies have found no significant differences between TIVA and IA. For example, in patients with esophageal cancer, overall survival did not differ according to the anesthetic technique used (20). Similarly, another study found no significant difference in overall survival or disease-free survival between total intravenous anesthesia and inhalational anesthesia in pancreatic cancer patients (15).

This study has certain limitations that should be noted. As it is a retrospective cohort study, there is a risk of selection bias in the choice of anesthetic technique, as well as possible uncontrolled confounding factors. Also, the sampling was non-probabilistic, which may limit the generalizability of the findings beyond the study population and the data obtained come from a private clinic, which makes it more difficult to extrapolate the conclusions to the general healthcare system. Furthermore, the lack of standardization in adjuvant cancer treatments limits the possibility of attributing direct causality to the anesthetic technique. Furthermore, there may have been unmeasured confounding variables that could influence the observed associations. For instance, factors such as the surgeon's experience level and

delays in cancer diagnosis or treatment initiation were not available in the dataset and could impact patient outcomes.

Conclusion

Based on the results obtained in this study, it is suggested that TIVA could be a potentially safer alternative in terms of mortality and postoperative complications for patients undergoing cancer surgery. This potential benefit is particularly relevant considering that the anesthetic technique is a modifiable factor in perioperative management. Although the results suggest a possible benefit of TIVA over IA in terms of mortality, the lack of significance in the Cox model means that these findings should be interpreted with caution.

Abbreviations

- **ASA**

American Society of Anesthesiologists physical status classification

- **BMI**

Body Mass Index

- **CCI**

Charlson Comorbidity Index

- **CI**

Confidence Interval

- **HR**

Hazard Ratio

- **IA**

Inhalation Anesthesia

- **IRR**

Incidence Rate Ratio

- **RR**

Relative Risk

- **SD**

Standard Deviation

- **TIVA**

Total Intravenous Anesthesia

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Faculty of the Private University of Científica del Sur, granting it registration code 006-2025-PRO99, and Auna Ideas, granting it registration code 2025002.

All participants provided informed consent. The anonymity and confidentiality of the data were ensured throughout all phases of the study.

Consent for publication

Not applicable.

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Author Contribution

DMFD: Conceptualization, Methodology, Data collection, Data curation, Writing – protocol, original and final draft – revision and editing, approval of the final version. CAEF: Methodology, Data collection, Data curation, Writing – protocol, original and final draft– revision and editing, approval of the final version. SYM: Methodology, Data collection, Data curation, Writing – protocol, original and final draft – review and editing, approval of final version. YAB: Writing –original and final draft – revision and editing, approval of the final version. FRC: Supervision, Methodology, Statistical analysis, Writing – review and editing of protocol, original and final draft–, Approval of final version, Critical review of intellectual content. CQN: Writing –original draft – revision and editing, approval of the final version. NVCA: Writing –original and final draft – revision and editing, approval of the final version. MCVS: Writing –original and final draft – revision and editing, approval of the final version. BCTZ: Writing –original and final draft– revision and editing, approval of the final version. ICAM: Writing – review and editing of the protocol, original and final draft –, approval of the final version, critical review of the intellectual content. CFGB: Writing – review and editing of the protocol, original and final draft –, approval of the final version, critical review of the intellectual content.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

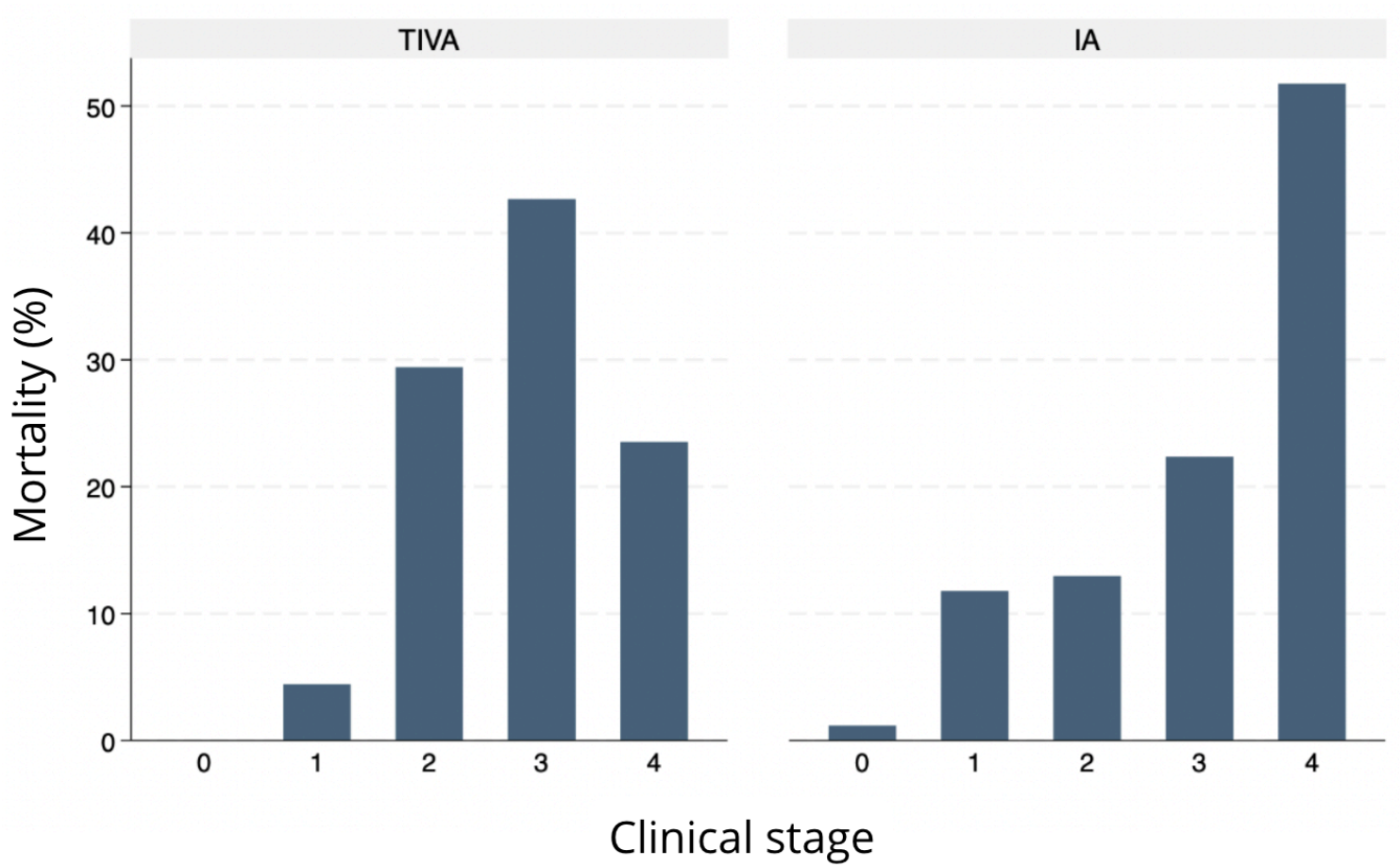


Figure 1

Percentage distribution of mortality in cancer patients by clinical stage, according to type of anesthesia

*TIVA: Total Intravenous Anesthesia. IA: Inhalation Anesthesia.

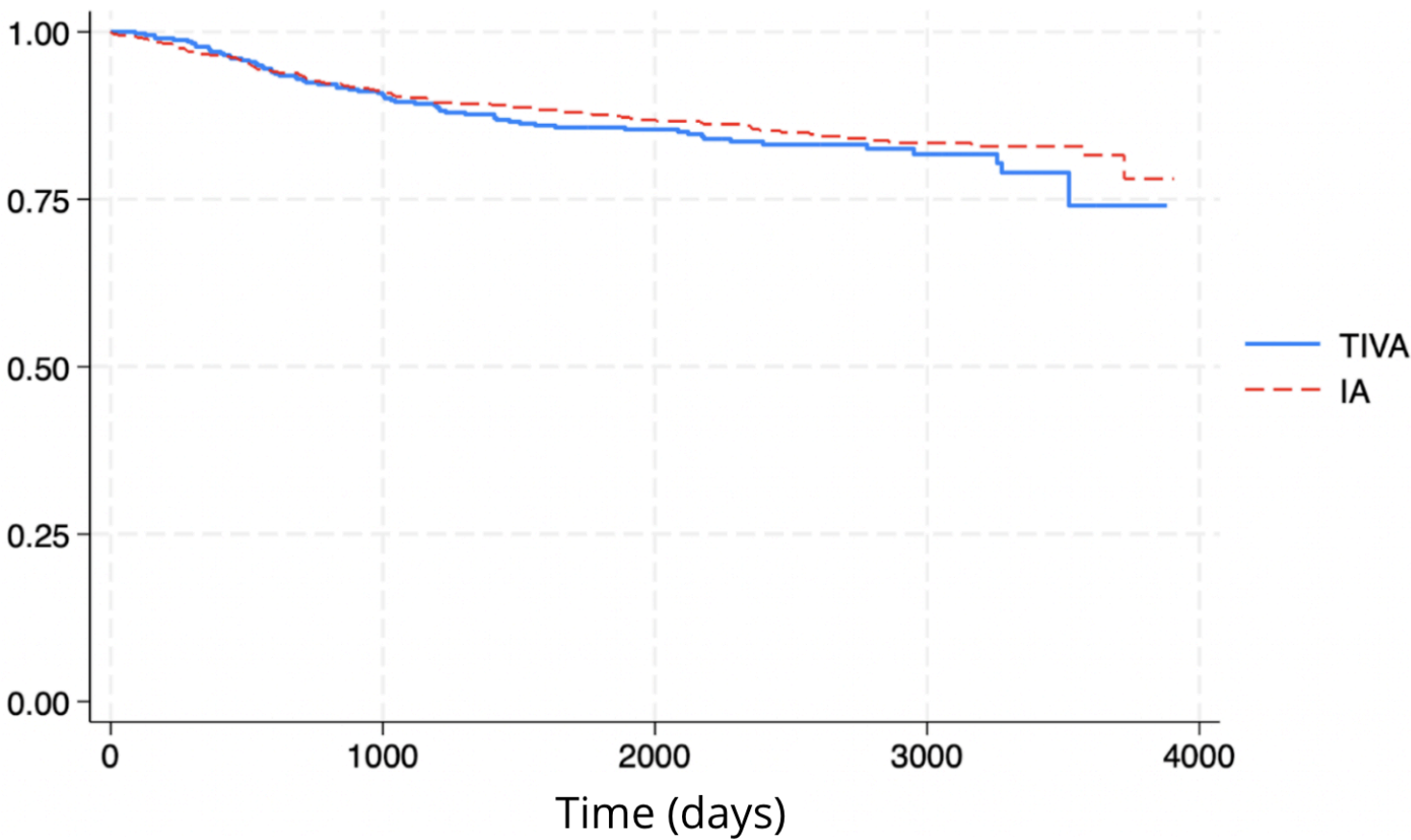


Figure 2
Kaplan-Meier survival curve according to type of anesthesia

Supplementary Files

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- [suppfile.docx](#)