Can J Anesth/J Can Anesth (2024) 71:95–106
https://doi.org/10.1007/s12630-023-02607-y

REPORTS OF ORIGINAL INVESTIGATIONS

Capnography access and use in Kenya and Ethiopia
Accès à et utilisation de la capnographie au Kenya et en Éthiopie

Maziar M. Nourian, MD · Amany Alshibli, MD · John Kamau, BSc · Susan Nabulindo, MD · Dennis A. Amollo, BSc · Jennifer Connell, BS · Svetlana K. Eden, PhD · Rahel Seyoum, MSc · Masresha G. Teklehaimanot, BSc · Gebrehiwot A. Tegu, MSc · Haftom B. Desta, MSc · Mark Newton, MD · Bantayehu Sileshi, MD

Received: 12 October 2022 / Revised: 30 May 2023 / Accepted: 1 June 2023 / Published online: 1 November 2023

Abstract

Purpose *Lack of access to safe and affordable anesthesia and monitoring equipment may contribute to higher rates of morbidity and mortality in low- and middle-income countries (LMICs). While capnography is standard in high-income countries, use in LMICs is not well studied. We evaluated the association of capnography use with patient and procedure-related characteristics, as well as the association of capnography use and mortality in a cohort of patients from Kenya and Ethiopia.*

Methods *For this retrospective observational study, we used historical cohort data from Kenya and Ethiopia from 2014 to 2020. Logistic regression was used to study the association of capnography use (primary outcome) with patient/procedure factors, and the adjusted association of intraoperative, 24-hr, and seven-day mortality (secondary outcomes) with capnography use.*

Results *A total of 61,792 anesthetic cases were included in this study. Tertiary or secondary hospital type (compared with primary) was strongly associated with use of capnography (odds ratio [OR], 6.27; 95% confidence interval [CI], 5.67 to 6.93 and OR, 6.88; 95% CI, 6.40 to 7.40, respectively), as was general (vs regional) anesthesia (OR, 4.83; 95% CI, 4.41 to 5.28). Capnography use was significantly associated with lower odds of intraoperative mortality in patients who underwent general anesthesia (OR, 0.31; 95% CI, 0.17 to 0.48). Nevertheless, fully-adjusted models for 24-hr and seven-day mortality showed no evidence of association with capnography.*

Conclusion *Capnography use in LMICs is substantially lower compared with other standard anesthesia monitors. Capnography was used at higher rates in tertiary centres*

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12630-023-02607-y.

M. M. Nourian, MD (✉)
Department of Anesthesiology, Vanderbilt University Medical Center, 1211 Medical Center Drive, Nashville, TN 37232, USA
e-mail: maziarnourian@gmail.com

A. Alshibli, MD
Department of Anesthesia and Perioperative Care, University of California at San Francisco, San Francisco, CA, USA

J. Kamau, BSc
African Mission Healthcare, ImPACT Africa-Tanzania, Nairobi, Kenya

S. Nabulindo, MD
Department of Anesthesiology, University of Nairobi, Nairobi, Kenya

D. A. Amollo, BSc
African Population and Health Research Center, Nairobi, Kenya

J. Connell, BS
Vanderbilt University School of Medicine, Nashville, TN, USA

S. K. Eden, PhD
Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, USA

R. Seyoum, MSc · G. A. Tegu, MSc
Department of Anesthesiology, Bahir Dar University, Bahir Dar, Ethiopia

M. G. Teklehaimanot, BSc · H. B. Desta, MSc
Department of Anesthesiology, Mekelle University, Mekelle, Ethiopia

M. Newton, MD · B. Sileshi, MD
Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, TN, USA

and with patients undergoing general anesthesia. While this study revealed decreased odds of intraoperative mortality with capnography use, further studies need to confirm these findings.

Résumé

Objectif *Le manque d'accès à des équipements d'anesthésie et de monitorage sécuritaires et abordables peut contribuer à des taux plus élevés de morbidité et de mortalité dans les pays à revenu faible et intermédiaire (PRFI). Alors que la capnographie est une modalité standard dans les pays à revenu élevé, son utilisation dans les PRFI n'est pas bien étudiée. Nous avons évalué l'association de l'utilisation de la capnographie avec les caractéristiques des patient·es et des interventions, ainsi que l'association de l'utilisation de la capnographie et de la mortalité dans une cohorte de patient·es du Kenya et d'Éthiopie.*

Méthode *Pour cette étude observationnelle rétrospective, nous avons utilisé des données de cohortes historiques du Kenya et de l'Éthiopie de 2014 à 2020. Une régression logistique a été utilisée pour étudier l'association entre l'utilisation de la capnographie (critère d'évaluation principal) et les facteurs patient·es/interventions, ainsi que pour étudier l'association ajustée entre la mortalité peropératoire, à 24 h et à sept jours (critères d'évaluation secondaires) et l'utilisation de la capnographie.*

Résultats *Au total, 61 792 cas d'anesthésie ont été inclus dans cette étude. Le type d'hôpital tertiaire ou secondaire (par rapport à un établissement primaire) était fortement associé à l'utilisation de la capnographie (rapport de cotes [RC], 6,27; intervalle de confiance [IC] à 95 %, 5,67 à 6,93 et RC, 6,88; IC 95 %, 6,40 à 7,40, respectivement), tout comme l'était l'anesthésie générale (vs régionale) (RC, 4,83; IC 95 %, 4,41 à 5,28). L'utilisation de la capnographie était significativement associée à une probabilité plus faible de mortalité peropératoire chez les patient·es ayant reçu une anesthésie générale (RC, 0,31; IC 95 %, 0,17 à 0,48). Néanmoins, les modèles entièrement ajustés pour la mortalité à 24 heures et à sept jours n'ont montré aucune donnée probante d'association avec la capnographie.*

Conclusion *L'utilisation de la capnographie dans les PRFI est considérablement moins répandue que celle d'autres moniteurs d'anesthésie standard. La capnographie a été utilisée à des taux plus élevés dans les centres tertiaires et chez des patient·es sous anesthésie générale. Bien que cette étude ait révélé une diminution de la probabilité de mortalité peropératoire avec l'utilisation de la capnographie, d'autres études doivent confirmer ces résultats.*

Keywords capnography · end-tidal carbon dioxide · low-resource-settings · perioperative mortality

Background

Five billion people lack access to safe, affordable, and timely surgery and anesthesia care.[1] When care is available, perioperative mortality in low- and middle-income countries (LMICs) remains relatively high. Specifically, anesthesia-related mortality in LMICs is 1,000-times greater than in high-income countries.[2] Part of this disparity could be due to a lack of reliable anesthesia technology, including monitoring equipment.[2] In addition to other essential monitors, the World Federation of Societies of Anesthesiologists (WFSA), American Society of Anesthesiologists (ASA), and World Health Organization (WHO) all identify capnography as an essential monitor in anesthetic practice.[3,4]

Capnography is most commonly used in the operating room to confirm endotracheal intubation and to monitor ventilation; however, its use extends to other areas of the hospital such as intensive care units (ICUs), emergency departments, postanesthesia care units, and sedation suites.[5,6] Esophageal intubations, circuit disconnections, and circulatory collapse are among the many causes of morbidity and mortality that could be detected early with capnography. While these complications are rare, the consequences can be lethal.[7] A year-long United Kingdom National Health Service evaluation, the National Audit Project (NAP4), captured detailed reports of major complications of airway management from all National Health Service hospitals. This analysis revealed that lack of capnography use accounted for 82% of events leading to death or brain damage in the ICU setting, likely due to failure to recognize esophageal intubations and endotracheal tube displacements.[8]

Unfortunately, there are no randomized controlled trials during general anesthesia to show the importance of capnography for general anesthesia, nor is there conclusive evidence that increasing access to capnography improves patient outcomes, especially in LMICs.[9] Prior research has attempted to quantify access to capnography in LMICs. Jooste *et al.* aimed to identify the capnography gap in Malawi and furthermore quantify morbidity and mortality averted after distribution of capnography units.[10] Their findings revealed an esophageal intubation rate of 11.7 per million per year in Malawi and, after introduction of capnography, 90% of anesthesia providers thought lives had been saved (a minimum of 57 lives in a six-month period).

To better understand capnography use in LMICs, we performed a retrospective evaluation of a previously collected data set of over 51,761 anesthetic cases in Kenya and 10,203 in Ethiopia, collected between 2014 and 2020. Our goal is to show that, despite WFSA's identification of capnography as an essential monitor in anesthetic practice, capnography is not universally available in LMICs, with its use being lower in rural settings.[11] We aimed to identify capnography availability and the patient-/procedure-related characteristics associated with its use. We also evaluated perioperative mortality rates and their association with capnography, adjusted for patient-/procedure-related characteristics.

Materials and methods

Study design, setting, and data sources

This study used previously collected data through the Global Perioperative Outcomes database, as described in previous manuscripts.[12,13] The data collection methodology was approved by the Institutional Review Boards of Kenyatta National Hospital (July 2015; Nairobi, Kenya), Tibebe Ghion Specialized Hospital (October 2018; Bahir Dar, Ethiopia), Ayder Comprehensive Specialized Hospital (July 2018; Mekelle, Ethiopia), the Kijabe Hospital (September 2014, Kijabe, Kenya), and Vanderbilt University Medical Center (August 2014; Nashville, Tennessee, USA), without requiring written informed consent. Data were collected from 2014 to 2020 in Kenya and from 2018 to 2020 in Ethiopia. The hospitals included in the study were 32 hospitals from Kenya and nine hospitals from Ethiopia (Electronic Supplementary Material [ESM] eTable). For our analysis, we categorized hospitals into primary, secondary, and tertiary. These distinctions for the Kenyan hospitals included were published by Kenyan government officials and are determined by number of hospital beds and operating theatres in the hospital. We used similar hospital sizes to categorize the Ethiopian hospitals included in our study. These data were collected by primary anesthesia providers, and data collection was overseen by a data manager assigned to each site. The primary anesthesia providers entered data using an electronic tablet (optional offline entry), and the data manager collected follow-up data including mortality status up to seven days postoperatively. Data managers routinely performed quality assurance by cross-referencing collected data with data from hospital logbooks. These data were presented quarterly and monitored by the data quality team to ensure consistency of data collection. Lastly, deidentified case data were exported from the electronic database for analysis for this retrospective study. We included all available cases in the data set, including pediatric, general, and regional anesthesia cases.

The rate of capnography and/or other monitor use was defined as number of cases with the monitor used over the overall number of cases (with and without monitor use).

Questionnaire variables

As described in previous studies, a perioperative outcomes tool was created using a REDCap tool (Vanderbilt University, Nashville, TN, USA) for all participating hospitals. This database contains 132 standardized data fields covering patient demographics, general case information, anesthetic type, intraoperative complications, as well as a follow-up course detailed below.[12–14] Intraoperative complications (including intraoperative death) were collected by anesthesia providers and included any airway, cardiovascular, or miscellaneous injuries to the patient. The data for postoperative mortality were collected by data managers either by using the hospital's mortality log while the patient was admitted or by making a follow-up phone call to the patient or designated family member up to seven days after the operation. The rate of death reported on postoperative day (POD) 7 was a cumulative rate of death one week after an operation. Death rates at POD 1 and POD 7 were collected by data managers in a similar and consistent fashion in all hospitals.

For this study, we extracted and analyzed all surgical cases available in the database and analyzed and reported the rate of capnography use in various settings and the patient demographics.

Statistical analysis

We summarized patient-/procedure-related characteristics by capnography use using counts and proportions (all characteristics were categorical). Pearson's Chi square test was used to compare the groups with and without capnography. We report unadjusted capnography rates (overall) and mortality rates (overall and stratified by capnography) and their 95% confidence intervals (CIs) computed using Wilson's method.

Our primary outcome was capnography use. To study the association of capnography use with patient-/procedure-related characteristics, we used logistic regression with capnography (yes/no) as an outcome and the following patient-/procedure-related characteristics as covariates: ASA Physical Status (I, II, III+), sex, country (Kenya, Ethiopia), categorical age ($\geq$ 65 yr, 18 yr to $<$ 65 yr, 12 yr to $<$ 18 yr, 3 yr to $<$ 12 yr, 3 months to $<$ 3 yr, $<$ 3 months), procedure (orthopedic, Cesarean delivery, general surgery, other), emergency (yes, no), airway management (endotracheal tube [ETT], fibreoptic bronchoscope, cricothyroidotomy, supraglottic airway [SGA], supplemental oxygen, no airway management), anesthesia type (general, regional, other [local anesthesia, sedation with or without local anesthesia]), and hospital type (primary, secondary, tertiary). We report the odds ratios (ORs) and 95% CIs of capnography receipt for each of the preceding patient-/procedure-related characteristics.

Our secondary outcomes were seven-day, 24-hr, and intraoperative mortality. Based on our previous work, missing mortality was assumed to be missing completely at random.[13] Because the association between capnography and mortality can be confounded by patient-/procedure-related characteristics, to study the associations of seven-day and 24-hr mortality, we included the same covariates as the model for capnography (see previous paragraph). Because published literature[9] suggests that the association of capnography and mortality may differ for different anesthesia types, we also included the interaction term of capnography and anesthesia type. To study the association between intraoperative mortality and capnography, we also used logistic regression. Nevertheless, because of the small number of events, in addition to capnography, we could only adjust for anesthesia type and its interaction to avoid overfitting.[15] For each of the preceding models, we report the ORs and 95% CIs of mortality for patients who received capnography *vs* those who did not, stratified by the anesthesia type. We also report the ORs and 95% CIs of mortality for all covariates.

Missing covariate values were imputed using predictive mean matching and multiple imputation with chained equations,[16,17] resulting in ten imputed data sets. These ten models were combined using Rubin's rule.[18] To assess the magnitude of potential unobserved confounding, we performed sensitivity analyses using E-values.[19] Across all analyses, the type I error rate of 0.05 was used. Analyses were performed using R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).[20]

Results

After excluding 172 individuals (because of missing airway technique), a total of 61,792 cases were included in this study, the majority of which (51,609; 84%) were performed in Kenya and the remainder in Ethiopia (Table 1). Of the cases, 12,656 (20%) were conducted in a tertiary setting, 12,056 (20%) in a primary setting, and 37,080 (60%) in a secondary setting. Most cases (46,901; 77%) were performed in adults (> 8 yr old), with a roughly equal distribution between male and female. A vast majority of cases were performed in healthy patients with ASA Physical Status of I and II (57,263, 94%). Twenty-eight thousand, six hundred and fifty-nine cases (47%) were performed under general anesthesia, whereas 46% were performed under regional anesthesia. Of the cases that were performed under general anesthesia, 440 (0.02%) were conversions to general from spinal/regional and 227 (0.01%) were combined nerve block and general cases. Neuraxial anesthesia (spinal and/or epidural) was used in 27,243 (46%) of cases, with sedation comprising 3,413 (6%), peripheral nerve blocks comprising 574 (0.9%), and local anesthesia infiltration comprising 947 (2%) of cases. Of the cases reported, 21,067 (35%) were reported as emergent and 8,868 (15%) were deemed to be trauma, a phenomenon common to surgical case load in low-resource settings.

There was a fairly even split between Cesarean delivery, abdominal general surgery, and orthopedic cases, as seen in Table 1. Of the cases, 26,352 (43%) used airway management beyond supplemental oxygen (SGA placement, ETT placement, or fibreoptic intubation). Lastly, capnography was used in 25,842 (42%) of cases. Other standard ASA monitors are displayed in Table 1 for comparison. Out of 35,950 cases without capnography use, 34,221 (95%) patients had oximetry used. The rate of missing data was 0% for capnography monitoring and intraoperative mortality, while 5,076 cases (8%) were missing 24-hr mortality follow-up and 11,997 cases (19%) were missing seven-day mortality follow-up. For other variables, missing counts (percentages of total counts) were 955 (2%) for ASA Physical Status, 1,952 (3%) for sex, 1,111 (2%) for age, 741 (1%) for procedure type, 912 (2%) for emergency, 978 (2%) for anesthesia type, and 0 (0%) for hospital type.

Figure 1 shows the results of the primary analysis. Hospital type was the most important factor associated with capnography use; specifically receiving care in the secondary or tertiary *vs* primary hospital was associated with much higher odds of capnography use (OR, 6.88; 95% CI, 6.40 to 7.40 and OR, 6.27; 95% CI, 5.67 to 6.93, respectively). The second important associated factor with capnography use was anesthesia type. Receiving general *vs* regional anesthesia was associated with higher odds of capnography use (OR, 4.83; 95% CI, 4.41 to 5.28), while receiving local anesthesia and/or sedation *vs* regional anesthesia was associated with lower odds of capnography use (OR, 0.85; 95% CI, 0.77 to 0.93). There was no evidence that sex and ASA Physical Status were associated with capnography use (*P* values of 0.72 and 0.57, respectively). Lastly, compared with adults (18–65 yr old), capnography was associated with higher odds of being used in children aged three months to three years (OR, 1.37; 95% CI, 1.24 to 1.52) and in children younger than three months (OR, 1.5; 95% CI, 1.3 to 1.71).

Table 1 Patient characteristics stratified by capnography

	N	No capnography *N* = 35,950	Capnography *N* = 25,842	Total *N* = 61,792	*P* value
Hospital type	61,792				< 0.001
Primary		10,750/35,950 (30%)	1,306/25,842 (5%)	12,056/61,792 (20%)	
Secondary		18,669/35,950 (52%)	18,411/25,842 (71%)	37,080/61,792 (60%)	
Tertiary		6,531/35,950 (18%)	6,125/25,842 (24%)	12,656/61,792 (20%)	
Country	61,792				0.23
Kenya		29,971/35,950 (83%)	21,638/25,842 (84%)	51,609/61,792 (84%)	
Ethiopia		5,979/35,950 (17%)	4,204/25,842 (16%)	10,183/61,792 (16%)	
Age	60,681				< 0.001
≥ 65 yr		3,308/35,950 (9%)	2,147/25,842 (8%)	5,455/61,792 (9%)	
18 yr to < 65 yr		26,962/35,950 (76%)	14,484/25,842 (57%)	41,446/61,792 (68%)	
12 yr to < 18 yr		2,139/35,950 (6%)	1,437/25,842 (6%)	3,576/61,792 (6%)	
3 yr to < 12 yr		1,732/35,950 (5%)	3,426/25,842 (13%)	5,158/61,792 (9%)	
3 months to < 3 yr		721/35,950 (2%)	2,585/25,842 (10%)	3,306/61,792 (5%)	
< 3 months		403/35,950 (1%)	1,337/25,842 (5%)	1,740/61,792 (3%)	
Sex	59,840				< 0.001
Male		13,086/35,950 (37%)	12,767/25,842 (51%)	25,853/61,792 (43%)	
Airway management	61,792				< 0.001
None		2,422/35,950 (7%)	397/25,842 (2%)	2,819/61,792 (5%)	
Room air or supplemental oxygen		26,935/35,950 (75%)	5,686/25,842 (22%)	32,621/61,792 (53%)	
Laryngeal mask airway		672/35,950 (2%)	2,385/25,842 (9%)	3,057/61,792 (5%)	
Endotracheal intubation (laryngoscopy, fibreoptic, and/or cricothyrotomy)		5,921/35,950 (16%)	17,374/25,842 (67%)	23,295/61,792 (38%)	
Emergency case	60,880				< 0.001
Yes		16,434/35,950 (47%)	4,633/25,842 (18%)	21,067/61,792 (35%)	
Trauma	60,505				< 0.001
Yes		5,757/35,950 (16%)	3,111/25,842 (12%)	8,868/61,792 (15%)	
ASA Physical Status	60,837				< 0.001
I		14,284/35,950 (40%)	11,652/25,842 (46%)	25,936/61,792 (43%)	
II		19,372/35,950 (55%)	11,955/25,842 (47%)	31,327/61,792 (51%)	
III+		1,766/35,950 (5%)	1,808/25,842 (7%)	3,574/61,792 (6%)	
Anesthesia type	60,814				< 0.001
General anesthesia		7,650/35,950 (22%)	21,009/25,842 (81%)	28,659/61,792 (47%)	
Regional anesthesia (spinal and epidural)		23,814/35,950 (68%)	3,990/25,842 (15%)	27,804/61,792 (46%)	
Peripheral nerve block only		450/35,950 (1%)	124/25,842 (0.5%)	574/61,792 (0.9%)	
Peripheral nerve block and general		64/35,950 (0.2%)	163/25,842 (0.6%)	227/61,792 (0.4%)	
Sedation with or without local anesthesia		2,769/35,950 (8%)	635/25,842 (2%)	3,404/61,792 (6%)	
Local anesthesia only		799/35,950 (2%)	148/25,842 (0.6%)	947/61,792 (2%)	
Spinal/regional converted to general		182/35,950 (0.5%)	258/25,842 (1%)	440/61,792 (0.7%)	
Procedure group	61,051				< 0.001
Cesarean delivery		13,330/35,950 (38%)	1,769/25,842 (7%)	15,099/61,792 (25%)	
General surgery		6,117/35,950 (17%)	7,825/25,842 (30%)	13,942/61,792 (23%)	
Orthopedic surgery		8,012/35,950 (23%)	4,080/25,842 (16%)	12,092/61,792 (20%)	
Other		7,842/35,950 (22%)	12,076/25,842 (47%)	19,918/61,792 (33%)	
Airway attempts	27,392				< 0.001
1		16,819/35,950 (72%)	2,740/25,842 (67%)	19,559/61,792 (71%)	
2		5,309/35,950 (23%)	1,046/25,842 (26%)	6,355/61,792 (23%)	
3 or more		1,197/35,950 (5%)	281/25,842 (7%)	1,478/61,792 (5%)	

Table 1 continued

	N	No capnography N = 35,950	Capnography N = 25,842	Total N = 61,792	P value
Pulse oximeter	61,792				< 0.001
Used		34,221/35,950 (95%)	25,732/25,842 (100%)	59,953/61,792 (97%)	
End-tidal CO_2 (capnography)	61,792				< 0.001
Used		0/35,950 (0.0%)	25,842/25,842 (100%)	25,842/61,792 (42%)	
Blood pressure cuff	61,792				< 0.001
Used		33,616/35,950 (94%)	25,148/25,842 (97%)	58,764/61,792 (95%)	
Electrocardiogram	61,792				< 0.001
Used		19,157/35,950 (53%)	23,731/25,842 (92%)	42,888/61,792 (69%)	
Temperature probe	61,792				< 0.001
Used		2,072/35,950 (6%)	4,744/25,842 (18%)	6,816/61,792 (11%)	
Stethoscope	61,792				< 0.001
Used		9,850/35,950 (27%)	14,101/25,842 (55%)	23,951/61,792 (39%)	
Peripheral nerve stimulator	61,792				< 0.001
Used		172/35,950 (0.5%)	390/25,842 (2%)	562/61,792 (0.9%)	

ASA = American Society of Anesthesiologists

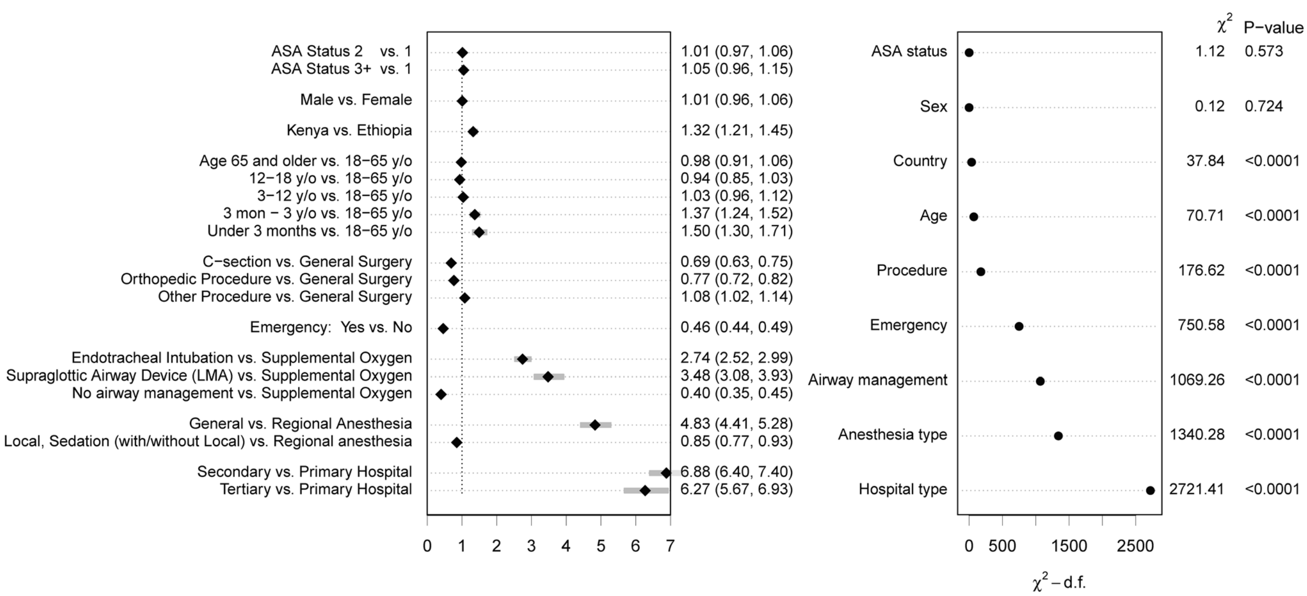

Fig. 1 Model results for capnography use. Left: adjusted associations (odds ratios and 95% confidence intervals) of capnography use and case characteristics in the order of increasing association strength. Right: variable association strength (Chi square test statistics minus degrees of freedom) and P values.
ASA = American Society of Anesthesiologists; LMA = laryngeal mask airway (LMA™ is a trademark of Teleflex Incorporated [Wayne, PA, USA] or its affiliates); y/o = years old

The overall intraoperative mortality rate was 51 (0.1%), while 24-hr and seven-day mortality rates were 406 (0.7%) and 649 (1%), respectively (Table 2).

Figure 2 shows adjusted ORs of mortality for patients with *vs* without capnography stratified by anesthesia type. The models for seven-day and 24-hr mortality showed no evidence of association of mortality and capnography

Table 2 Unadjusted mortality rates stratified by capnography use

	N	No capnography *N* = 35,950	Capnography *N* = 25,842	Total *N* = 61,792	*P* value
Intraoperative mortality	61,792	31 (0.1%)	20 (0.1%)	51 (0.1%)	0.71
24-hr mortality	56,716	223 (0.6%)	183 (0.7%)	406 (0.7%)	0.28
Seven-day mortality	49,795	307 (0.9%)	342 (1%)	649 (1%)	< 0.001

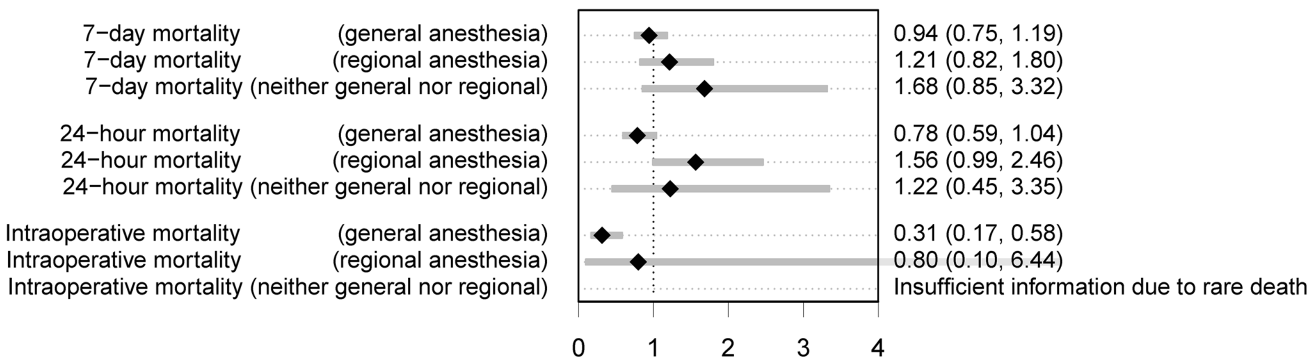

Fig. 2 Adjusted associations (odds ratios and 95% confidence intervals) of capnography use and mortality stratified by anesthesia type

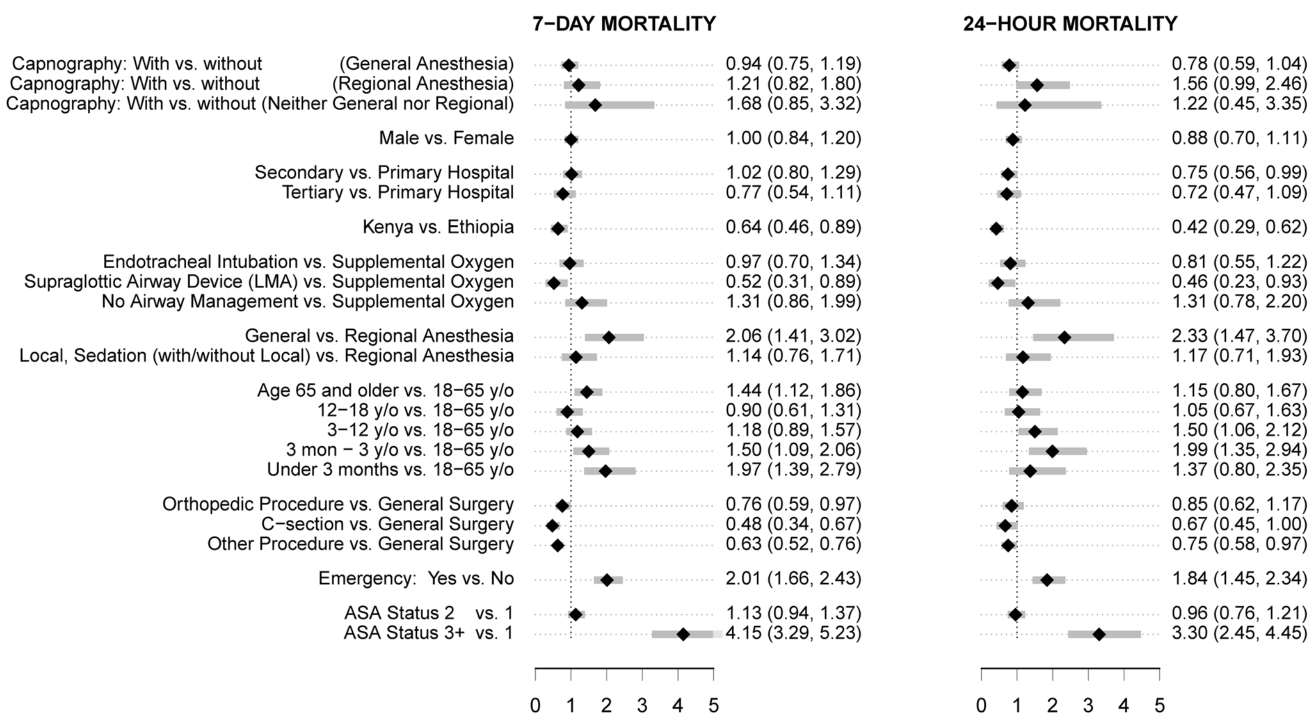

Fig. 3 Adjusted associations (odds ratios and 95% confidence intervals) of capnography with 24-hr and seven-day mortality
ASA = American Society of Anesthesiologists; LMA = laryngeal mask airway (LMA™ is a trademark of Teleflex Incorporated [Wayne, PA, USA] or its affiliates); y/o = years old

(P = 0.32 and 0.07, respectively) regardless of anesthesia type. The association of intraoperative mortality and capnography, however, was significant (P = 0.003); specifically, among patients who received general anesthesia, capnography use was associated with lower odds of intraoperative death (OR, 0.31; 95% CI, 0.17 to 0.58).

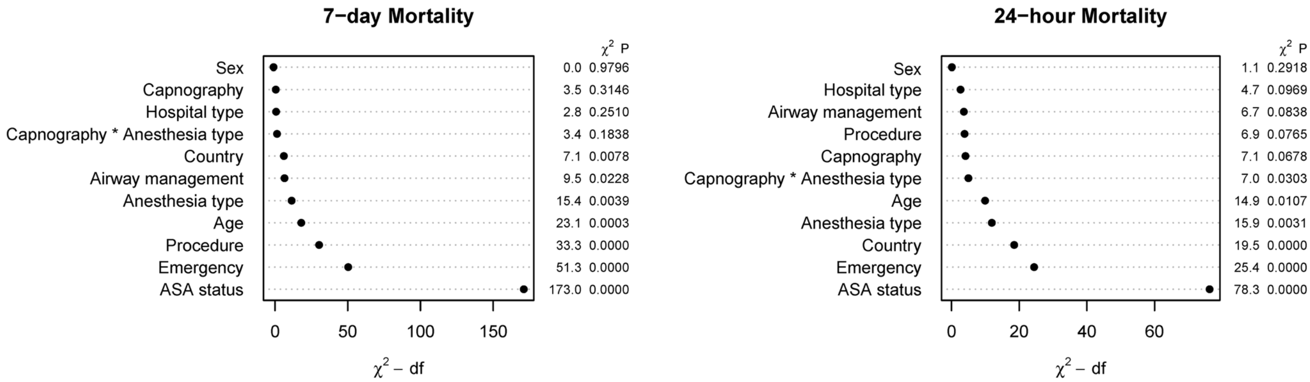

Fig. 4 Adjusted associations of 24-hr and seven-day mortality
ASA = American Society of Anesthesiologists

The sensitivity analysis using E-values showed that the OR of 0.31 with lower confidence bound of 0.17 could be explained away by a confounder with a risk ratio for both capnography and mortality of 2.83.

Figure 3 displays the adjusted associations of capnography with 24-hr and seven-day mortality in the order of variable association strength. Figure 4 shows the association strength of variables on 24-hr and seven-day mortality, which was consistent with that of previous studies.[21] The most associated factors for 24-hr and seven-day mortality included ASA Physical Status and emergency status.

Lastly, an unadjusted temporal trend of capnography and oximetry use are displayed in the ESM eFigure. The temporal trends reveal similarly high rates of pulse oximetry use over time (over 95%) and fluctuating rates of capnography use with the highest use in 2019 (about 55%) and the lowest use in 2017–2018 (about 35%).

Discussion

Capnography is a patient monitoring tool with a variety of uses, including emergency response, sedation, and respiratory monitoring for both intubated and non-intubated patients in the operating room, the postanesthesia care unit, and ICUs. The rate of capnography access and use is largely unknown in low-resource settings; however, a few estimates have been made that the capnography gap (lack of access) is approximately 45% in Indonesia,[22] 97% in Malawi,[10] and 100% in Madagascar.[23] In a scoping review assessing the impact of capnography on patient safety, only 6.5% of the published studies came from LMICs.[8] To our knowledge, our study is the largest database assessing rates of capnography use and access given various patient and hospital factors from a LMIC setting. In this study, we identify three main findings with regard to capnography access and use and present postoperative mortality rates in Kenya and Ethiopia.

First, capnography was only used in about 42% of total anesthetics. Factors that were most associated with capnography use were cases performed in secondary or tertiary hospitals, patients undergoing general anesthesia, use of more invasive airway devices, and cases with children under three months of age. Second, when compared with other ASA monitors and/or monitors recommended by WHO-WFSA such as pulse oximetry, we saw large differences in the rate of adoption and use perhaps because of the technical challenges of creating a low-cost capnograph for resource-poor settings.[24] Finally, there remain differences in overall mortality rate intraoperatively, at POD 1, and at POD 7 in Kenya and Ethiopia between anesthetic modalities.

Use of capnography requires not only special equipment but also understanding of waveform analysis, and certain technological and educational factors, such as adequate training, reliance on disposables, and maintenance of sampling pumps, that may prohibit the widespread distribution of machines.[10] As a result, it is more common to find capnography units in tertiary or urban hospitals than in rural hospitals.[25]

This study shows that in both Kenya and Ethiopia, only 10% of primary hospitals used capnography compared with almost 48% of tertiary hospitals. Adjusted analysis showed that procedures performed in a secondary or tertiary centre were associated with higher odds of capnography use (Fig. 1). This may be in part due to better funding and access to educational resources regarding proper capnography use. This lack of access to capnography presents unique challenges in rural hospital settings in terms of timely detection of esophageal intubations and early detection of circuit disconnection.[9] Additionally, use of capnography was associated with much higher odds of using an invasive airway management approach (SGA insertion or tracheal intubation). This is consistent with observations made by the authors that capnography is underused or not routinely used in regional anesthesia and/or sedation cases.

Additionally, capnography was used in only 18% of emergency cases and in 12% of trauma cases for all surgeries combined in Ethiopia and Kenya. Adjusted analysis showed lower odds of capnography use associated with emergency cases (Fig. 1). This is likely due to lack of availability or ease of access in a trauma or emergent setting. The airway and ventilation management required for both emergency and trauma cases presents unique challenges without available capnography. Out of 21,067 emergent cases, nine patients had an intraoperative death with capnography and 24 without.

In this study, it was also shown that being younger than three years was associated with a higher odds of capnography use. The authors speculate that this is likely due to the predicted tenuous respiratory physiology in a child and a larger possibility of endotracheal tube dislodgement during surgery in infants. Increasing capnography use in pediatric surgery is one possible way to decrease pediatric preoperative mortality. A recent multinational prospective cohort study in sub-Saharan Africa revealed significantly higher mortality rates for common surgical procedures, particularity in neonates.[12,26] Some of the cited factors for increased mortality include hospital-level deficiencies in monitoring equipment, such as an apnea monitor. In the PediPIPES study in West Africa, an apnea alarm detector/apnea monitor was only reported in 35% of hospitals. It is proposed that capnography can serve as an alternative apnea monitor.[27] Efforts, such as the Smile Train-LifeBox Capnography project, have already begun with aims to improve anesthesia safety for children in low-resource settings through better access to capnography.[28]

As an advocate for increased access to affordable capnography, the WFSA cites capnography as a highly recommended technology in both intubated and nonintubated sedated or anesthetized patients.[29] The rationale behind this stance is that capnography use is likely associated with a reduction in serious respiratory complications and improving access to capnography in LMICs may improve perioperative mortality.[9]

There was hope that capnography could emulate the successful closing of the pulse oximetry gap through improved access and use.[30] Devices distributed by LifeBox revolutionized pulse oximetry access. They have been effectively introduced into resource-poor operating rooms, with almost 20,000 devices distributed and used around the world.[31,32] Nevertheless, attention must be drawn to how we as a community can increase access to capnography either through innovation, establishment of standards and guidelines, or partnership with industry to improve surgical outcomes generally and access to context-appropriate capnography specifically.[24,29,33] Capnography has been discussed in the literature as a tool useful for detecting esophageal intubations and preventing morbidity and mortality in general anesthesia cases; it is recognized as one of many factors that need to be addressed to improve anesthetic care in resource-poor settings.[9,34]

While no prospective controlled trials have compared the use of capnography *vs* lack of capnography in general anesthesia, we can look at retrospective data and closed claims to speculate if capnography can improve patient outcomes and reduce perioperative mortality and morbidity. Furthermore, the adoption and integration of pulse oximetry globally represents a success story in mitigating the disparity in anesthetic monitoring between high-income countries and LMICs. We believe that if technology and distribution were to facilitate a similar path for capnography, it may ultimately improve patient outcomes.

Lastly, perioperative mortality in Africa, specifically in the postoperative period, is twice the global average for a multitude of factors.[21] A lack of access to proper and safe anesthesia equipment may contribute to a higher rate of postoperative death and complications. While there are many potential reasons for perioperative mortality, these data reveal a perioperative mortality rate one day after surgery of approximately 1:1,000 in Kenya and Ethiopia combined. These results are similar to other studies of 1:1,925 in a university teaching hospital in Zambia and 1:482 in a district hospital in Zimbabwe.[35,36] Unfortunately, these postoperative mortality rates are much higher compared with a mortality rate of 1:185,000 in the UK,[37] likely because of lack of access to equipment, trained personnel, and/or outcome-reporting systems.[38]

In this study, we present an adjusted analysis of association between capnography and mortality stratified by anesthesia type. During general anesthesia cases, there appears to be a trend of lower odds of mortality associated with capnography use, which tends to dissipate by POD 7. This trend, however, may be explained by the fact that intraoperative mortality is included in both 24-hr and seven-day mortality. While an intraoperative complication that could have led to intraoperative death may be related to the lack of patient monitoring (such as capnography), because data on possible confounding factors were absent, it is difficult to rule out other causes for mortality. Although our results show that capnography was associated with a lower rate of intraoperative mortality in patients who had capnography during general anesthesia, the model for intraoperative mortality was adjusted only for two variables (due to small effective sample size); therefore, the results may be biased due to confounding. Our sensitivity analysis with E-values showed that this effect could be explained away by including a confounder with a risk ratio of 2.83 for both capnography and intraoperative mortality, suggesting that this association is likely to disappear after adjusting for the relevant confounders. The association of capnography and seven-day and 24-hr mortality was not significant. Although the OR for capnography use suggested it is associated with lower odds of 24-hr mortality for general anesthesia and higher odds of 24-hr mortality for regional anesthesia, these associations were not significant and could be biased because of unobserved confounding. For example, the anesthesia practitioner was concerned with the stability of a patient (unobserved confounder), so additional monitoring was used. The patients who received capnography with regional anesthesia are likely patients in whom there was clinical concern for inadequate ventilation and/or hemodynamic compromise.

While we cannot make definitive statements regarding the impact of capnography on mortality in low-resource settings, this large LMIC data set should serve as a stepping stone, or puzzle piece, for use in understanding the current capnography status and prompting future LMIC studies to research all factors specifically associated with lack of access to capnography.

Limitations

This study has several limitations. It is a retrospective observational study, and the results may be biased by unobserved confounders. For example, trauma is a plausible confounding variable since severe trauma cases may be at a higher risk of intraoperative mortality and capnography may not be available soon enough. Although the overall sample size was large, the intraoperative mortality outcome was very rare, which did not allow adjustment for the majority of the observed confounders.

Additionally, we could not comment on rates of intraoperative complications (i.e., hypoxia, hypotension, esophageal intubation) with and without capnography use because they were underreported. Here, we report capnography use, which may imply access to the technology but could also be related to adoption and use of available monitoring. In addition, when capnography is available, it is used in all general anesthesia cases. The use of capnography when regional anesthesia is employed varies depending on the practice of the anesthesia provider. As such, we are unable to comment on the rate of whether capnography was available but not used by the anesthesia provider.

Furthermore, the data presented are historical and therefore the level of evidence linking lack of capnography use and perioperative mortality is weak. We suggest further studies to evaluate perioperative morbidity and mortality in LMICs as the adoption and use of capnography becomes more widespread. Lastly, the data presented in this paper represent access to equipment as early as 2014 and access may have improved since then.

Conclusions

In conclusion, although capnography is an essential monitoring device recommended by the ASA and WHO-WFSA to perform safe anesthesia, it is notably absent in many operating rooms worldwide. This study aimed to identify the rates of capnography use, patient-/procedure-related factors associated with its use, and its association with mortality in Kenya and Ethiopia. Future studies should further quantify the capnography gap in LMICs and identify areas of improvement in capacity building and innovation, thereby strengthening access to this crucial monitoring tool.

Author contributions *Maziar M. Nourian* and *Bantayehu Sileshi* contributed to all aspects of this manuscript, including study conception and design; acquisition, analysis, and interpretation of the data; and drafting the article. *Amany Alshibli* contributed to analysis and interpretation of data and drafting of the article. *John Kamau*, *Susan Nabulindo*, *Denis Amollo*, *Rahel Seyoum*, *Masresha G. Teklehaimanot*, *Gebrehiwot A. Tegu*, and *Haftom B. Desta* contributed to data collection and analysis. *Jennifer Connell* contributed to data analysis and drafting the article. *Svetlana Eden* contributed to data analysis, data interpretation, and drafting the article. *Mark Newton* contributed to study conception and design and manuscript review. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgements The authors would like to acknowledge Phillis Ngure, Mercy Kithengi, Wycliffe Odhiambo, and Aziz Munubi for their work as data managers. In addition, the authors would like to acknowledge KRNA students at Kijabe Hospital and nonphysician anesthesia students at Ayder Hospital, Felege Hiwot Hospital, and Tibebe Ghion Hospital for helping with data collection. Lastly, the authors would like to acknowledge Martha Tanner for her editorial support.

Disclosures The authors declare that they have no conflicts of interest.

Funding statement This work was supported by grants from the GE Foundation and ELMA Foundation.

Editorial responsibility This submission was handled by Dr. Adrian Gelb, Guest Editor, *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*.

References

1. *Meara JG, Leather AJ, Hagander L, et al.* Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. Int J Obstet Anesth 2016; 25: 75–8. https://doi.org/10.1016/j.ijoa.2015.09.006
2. *Bharati SJ, Chowdhury T, Gupta N, Schaller B, Cappellani RB, Maguire D.* Anaesthesia in underdeveloped world: present scenario and future challenges. Niger Med J 2014; 55: 1–8. https://doi.org/10.4103/0300-1652.128146
3. *Eichhorn JH.* Review article: practical current issues in perioperative patient safety. Can J Anesth 2013; 60: 111–8. https://doi.org/10.1007/s12630-012-9852-z
4. *American Society of Anesthesiologists.* Practice guidelines for moderate procedural sedation and analgesia 2018: a report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology. Anesthesiology 2018; 128: 437–79. https://doi.org/10.1097/aln.0000000000002043
5. *Long B, Koyfman A, Vivirito MA.* Capnography in the emergency department: a review of uses, waveforms, and limitations. J Emerg Med 2017; 53: 829–42. https://doi.org/10.1016/j.jemermed.2017.08.026
6. *Nassar BS, Schmidt GA.* Capnography during critical illness. Chest 2016; 149: 576–85. https://doi.org/10.1378/chest.15-1369
7. *Chrimes N, Higgs A, Hagberg CA, et al.* Preventing unrecognised oesophageal intubation: a consensus guideline from the Project for Universal Management of Airways and international airway societies. Anaesthesia 2022; 77: 1395–415. https://doi.org/10.1111/anae.15817
8. *Cook TM, Woodall N, Frerk C.* Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: anaesthesia. Br J Anaesth 2011; 106: 617–31. https://doi.org/10.1093/bja/aer058
9. *Wollner E, Nourian MM, Booth W, et al.* Impact of capnography on patient safety in high- and low-income settings: a scoping review. Br J Anaesth 2020; 125: e88–103. https://doi.org/10.1016/j.bja.2020.04.057
10. *Jooste R, Roberts F, Mndolo S, et al.* Global Capnography Project (GCAP): implementation of capnography in Malawi—an international anaesthesia quality improvement project. Anaesthesia 2019; 74: 158–66. https://doi.org/10.1111/anae.14426
11. *Gelb AW, Morriss WW, Johnson W, Merry AF.* World Health Organization-World Federation of Societies of Anaesthesiologists (WHO-WFSA) international standards for a safe practice of anesthesia. Can J Anesth 2018; 65: 698–708. https://doi.org/10.1007/s12630-018-1111-5
12. *Newton MW, Hurt SE, McEvoy MD, et al.* Pediatric perioperative mortality in Kenya: a prospective cohort study from 24 hospitals. Anesthesiology 2020; 132: 452–60. https://doi.org/10.1097/aln.0000000000003070
13. *Sileshi B, Newton MW, Kiptanui J, et al.* Monitoring anesthesia care delivery and perioperative mortality in Kenya utilizing a provider-driven novel data collection tool. Anesthesiology 2017; 127: 250–71. https://doi.org/10.1097/aln.0000000000001713
14. *Alshibli AK, Teklehaimanot MG, Seyoum R, et al.* Changes in surgical volume and outcomes during the coronavirus disease 2019 pandemic at two tertiary hospitals in Ethiopia: a retrospective cohort study. Anesth Analg 2022; 134: 1297–307. https://doi.org/10.1213/ane.0000000000005946
15. *Harrell FE Jr.* Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis. New York: Springer; 2001.
16. *Zhang Z.* Multiple imputation with multivariate imputation by chained equation (MICE) package. Ann Transl Med 2016; 4: 30. https://doi.org/10.3978/j.issn.2305-5839.2015.12.63
17. *van Buuren S, Groothuis-Oudshoorn K.* mice: multivariate imputation by chained equations in R. J Stat Softw 2011; 45: 1–67. https://doi.org/10.18637/jss.v045.i03
18. *Little RJ, Rubin DB.* Statistical Analysis with Missing Data. New York: John Wiley & Sons, Inc.; 2002.
19. *VanderWeele TJ, Ding P.* Sensitivity analysis in observational research: introducing the E-value. Ann Intern Med 2017; 167: 268–74. https://doi.org/10.7326/m16-2607
20. *The R Foundation.* R: the R Project for statistical computing. Available from URL: https://www.R-project.org/ (accessed June 2023).
21. *Biccard BM, Madiba TE, Kluyts HL, et al.* Perioperative patient outcomes in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. Lancet 2018; 391: 1589–98. https://doi.org/10.1016/s0140-6736(18)30001-1
22. *Ramlan AA, Lestari MI, Banadji Y, Arif SK.* A national survey of capnography utilization among anaesthesiologists in Indonesia. Trends Anaesth Crit Care 2021; 40: 9–13. https://doi.org/10.1016/j.tacc.2021.06.004
23. *Baxter LS, Ravelojaona VA, Rakotoarison HN, et al.* An observational assessment of anesthesia capacity in madagascar as a prerequisite to the development of a national surgical plan. Anesth Analg 2017; 124: 2001–7. https://doi.org/10.1213/ane.0000000000002049
24. *Nourian MM, Kolbay P, Hoehne S, et al.* Investigating capnography innovation for better patient monitoring in the resource limited surgical setting. Surg Innov 2019; 26: 124–8. https://doi.org/10.1177/1553350618813252
25. *Brouillette MA, Aidoo AJ, Hondras MA, et al.* Anesthesia capacity in Ghana: a teaching hospital's resources, and the national workforce and education. Anesth Analg 2017; 125: 2063–71. https://doi.org/10.1213/ane.0000000000002487
26. *PaedSurg Africa Research Collaboration.* Paediatric surgical outcomes in sub-Saharan Africa: a multicentre, international, prospective cohort study. BMJ Glob Health 2021; 6: e004406. https://doi.org/10.1136/bmjgh-2020-004406
27. *Kodali BS.* Capnography in pediatrics. Available from URL: https://www.capnography.com/pediatrics (accessed June 2023).
28. *Lifebox Foundation.* Smile Train and Lifebox launch request for proposals for capnography device. Available from URL: https://www.lifebox.org/news/capnography-device-rfp/ (accessed June 2023).
29. *Gelb AW, McDougall RJ, Gore-Booth J, Mainland PA, WFSA Ad Hoc Capnometry Workgroup.* The World Federation of Societies of Anaesthesiologists minimum capnometer specifications 2021—a guide for health care decision makers. Anesth Analg 2021; 133: 1132–7. https://doi.org/10.1213/ane.0000000000005682
30. *Funk LM, Weiser TG, Berry WR, et al.* Global operating theatre distribution and pulse oximetry supply: an estimation from reported data. Lancet 2010; 376: 1055–61. https://doi.org/10.1016/s0140-6736(10)60392-3
31. *Albert V, Mndolo S, Harrison EM, O'Sullivan E, Wilson IH, Walker IA.* Lifebox pulse oximeter implementation in Malawi: evaluation of educational outcomes and impact on oxygen desaturation episodes during anaesthesia. Anaesthesia 2017; 72: 686–93. https://doi.org/10.1111/anae.13838
32. *Lifebox Foundation.* Our work. Available from URL: https://www.lifebox.org/our-work/ (accessed June 2023).

33. *Lifebox Founadtion.* Smile Train—Lifebox safe surgery and anesthesia initiative. Available from URL: https://www.lifebox.org/smiletrain/ (accessed June 2023).
34. *Lipnick MS, Mavoungou P, Gelb AW.* The global capnography gap: a call to action. Anaesthesia 2019; 74: 147–50. https://doi.org/10.1111/anae.14478
35. *Enohumah KO, Imarengiaye CO.* Factors associated with anaesthesia-related maternal mortality in a tertiary hospital in Nigeria. Acta Anaesthesiol Scand 2006; 50: 206–10. https://doi.org/10.1111/j.1399-6576.2006.00945.x
36. *Glenshaw M, Madzimbamuto FD.* Anaesthesia associated mortality in a district hospital in Zimbabwe: 1994 to 2001. Cent Afr J Med 2005; 51: 39–44.
37. *Buck N, Devlin HB, Lunn JN.* The Report of a Confidential Enquiry into Perioperative Deaths. London: The Nuffield Trust; 1987.
38. *Walker I, Wilson I, Bogod D.* Anaesthesia in developing countries. Anaesthesia 2007; 62: 2–3. https://doi.org/10.1111/j.1365-2044.2007.05288.x