

## Knowledge and practice of opioid-free anaesthesia for non-bariatric surgery in an academic hospital: A cross-sectional study.

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### Abstract

#### Background:

The liberal use of opioids peri-operatively is a matter of concern in contemporary medical practice and carries the risk of numerous potentially undesirable effects. Multimodal Opioid-Free Anaesthesia (OFA) has been proven to reduce the incidence of the potentially undesirable effects of opioids beyond the initial premise of bariatric surgery.

#### Methods:

This descriptive, contextual, cross-sectional study was conducted from February 2022 through to February 2023. The study population was limited to 224 anaesthesia providers working in academic hospitals affiliated to the University of the Witwatersrand (Wits) Department of Anaesthesiology. The data for this study were collected by distributing an online questionnaire, which was formulated based on the available literature to ensure content validity. Data extracted included: years of anaesthetic experience, professional rank, affiliated Hospital, special training in OFA, and the answers to various aspects of knowledge and practice of OFA.

#### Results:

143 anaesthesia providers participated in the study. A statistically significant difference in OFA knowledge level was observed among the hospitals, as determined by the Kruskal-Wallis test ( $H = 13.9$ ,  $p = 0.046$ ). Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) had the highest percentage of respondents with knowledge of OFA, 38.5% and 25.9%, respectively. A significant number of participants reported not having any knowledge of OFA protocols ( $p = 0.030$ ); additionally, more participants indicated that their hospital did not have a formal OFA protocol ( $p < 0.001$ ).

#### Conclusion:

The study revealed a lack of knowledge of OFA for non-bariatric surgery and multiple challenges anaesthesia providers are confronted with in the adoption of OFA in clinical practice.

#### Recommendations:

Training programmes that mandate involvement in research activities, journal clubs, and CPD events focused on OFA. Hospital-specific OFA protocols based on resources available would encourage the practice of OFA.

**Keywords:** Opioid free anaesthesia; non-bariatric surgery; local anaesthetic systemic toxicity; opioids; pain management; opioid-related disorders; anaesthesia providers; perioperative care.

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### Introduction

The routine use of synthetic opioids, although rarely questioned, should be supported with evidence that favours patient outcomes in the perioperative period. The objective of the study was to describe the knowledge and

practice of OFA and to evaluate if there were any factors limiting the practice of OFA.

The principle of OFA is built on the additive and/or synergistic analgesic properties of different drugs while minimizing side-effects, particularly those of opioids<sup>1</sup>. Studies have shown that OFA fast-tracks surgery, reduces hospital stay, promotes early mobilization, and

earlier enteral nutrition<sup>1</sup>. Poor pain control affects the neuroendocrine stress response to surgery<sup>2</sup>. Reduced respiratory depression and decreased incidence of Post-Operative Nausea and Vomiting (PONV) were the most significant benefits of OFA. According to Basto T Machado,<sup>3</sup> nausea and vomiting significantly contribute to delayed patient recovery, and consequently delayed hospital discharge<sup>3</sup>.

According to Arain et al, OFA for major surgery reduces the early postoperative need for opioids by 66%<sup>4</sup>. Additionally, the use of non-opioid analgesic medications is a common theme of Enhanced Recovery After Surgery (ERAS) pathways, which have been shown to improve patient outcomes by reducing complication rates and length of hospital stay<sup>5</sup>.

In spine surgery, opioids can interfere with neurological monitoring. Post-craniotomy pain can be severe and is often not optimally managed. Local and regional anaesthesia can reduce or even eliminate the need for opioids peri-operatively. Pain scores two, four, six, eight, and 12 hours after scalp blocks show a significant opioid sparing benefit<sup>6</sup>. Patients undergoing thoracic surgery are at risk of severe pain, often managed with thoracic epidural analgesia. Bello et al<sup>7</sup> investigated the effect of OFA on epidural Ropivacaine requirements post thoracotomy. Within the first 48 postoperative hours, the cumulative epidural Ropivacaine consumption was significantly higher in the opioid-based anaesthesia group ( $p = 0.002$ ), and more of these patients required morphine compared to the OFA group (42% versus 4%,  $p < 0.05$ )<sup>7</sup>.

OFA is a pillar of the fast-track cardiac anaesthesia movement,<sup>8</sup> targeted at reducing time to extubation and length of hospital stay<sup>8</sup>. Two groups of drugs, Paracetamol, and anticonvulsants (Gabapentin and Pregabalin) have been reported to minimise opioid consumption when used preoperatively for cardiac surgery. According to Ochroch et al.<sup>(8)</sup> the use of Pregabalin preoperatively is associated with a 60% reduction in postoperative opioid requirement in patients undergoing off-pump coronary artery bypass graft (OPCAB).

OFA protocols have been described in different centres. Mulier and Sultana's methods are widely discussed. Mulier describes an infusion called Mulimix, which is described below<sup>9</sup>:

Pre-medication:

- Dexmedetomidine: 0.25 µg/kg ideal body weight (IBW), to a maximum dose of 20 µg.

Mulimix preparation:

- Dexmedetomidine 50 µg + Ketamine 50 mg + Lignocaine 500 mg diluted to 50 ml with 0.9% saline.

Induction:

- Mulimix 0.1 ml/kg IBW
- Propofol 2 mg/kg IBW
- Rocuronium 0.6–1.2 mg/kg IBW
- Add Magnesium Sulphate 40 mg/kg IBW

Maintenance of anaesthesia:

- Mulimix 0.1 ml/kg/hr IBW
- Propofol infusion or volatile agent

Sultana et al<sup>9</sup> described an alternative OFA protocol, adapted from Mulier's technique:

Pre-medication:

- Midazolam 2–3 mg
- Dexmedetomidine infusion 5 µg/kg/hr

Induction:

- Propofol 2 mg/kg IBW

Maintenance:

- Desflurane 0.5–1 minimum alveolar concentration (MAC)
- Dexmedetomidine 0.5–1 µg/kg/hr
- Paracetamol 20 mg/kg
- Non-steroidal anti-inflammatory drug (NSAID)
- Local wound infiltration
- Anti-emetic prophylaxis: Ondansetron and Dexamethasone

Opioid Sparing Anaesthesia (OSA):

Recommended when OFA is not feasible, such as when certain drugs are unavailable.

Mulier et al<sup>9</sup> adaptation for OSA:

Induction:

- Fentanyl 2 µg/kg
- Ketamine 0.2 mg/kg actual body weight (ABW)

Maintenance:

- Ketamine 0.1 mg/kg/hr ABW
- Lignocaine 1.5 mg/kg ABW/hr
- Remifentanyl 0.1–0.15 µg/kg ABW/min

## Objectives.

- To describe the knowledge and practice of OFA for non-bariatric surgery in an academic hospital.
- To describe the challenges encountered by anaesthesia providers in the practice of OFA.

## Methods

### Study population

This descriptive, contextual, cross-sectional study was limited to anaesthesia providers working in academic hospitals affiliated to the Wits Department of Anaesthesiology. 224 anaesthesia providers were offered to participate in the study. The staff complement of the department comprised 80 consultants, 114 registrars, 22 medical officers, and 8 career medical officers. The questionnaire was available online and could be completed without any time constraints. Participants who provided consent but didn't complete the questionnaire were reminded after 6 weeks had lapsed to minimise dropout. Data was collected from 1<sup>st</sup> February 2022 until 28<sup>th</sup> February 2023. The required sample size of 143 was determined using Raosoft™, accepting a margin of error of 5% with a confidence interval of 95%.

### Sample method

In this study, convenience sampling was used. Convenience sampling is a non-probability sampling method, which was considered appropriate for this descriptive study, where the first available primary data source was used for research without additional requirements.

### Inclusion criteria

- Medical officers
- Registrars
- Specialist anaesthetists

### Exclusion criteria

- Interns
- Community Service Medical Officers

### Data collection

The questionnaire was developed by the researchers based on the available literature to ensure content validity. The questionnaire was distributed to three senior specialist anaesthetists in the department to ensure face validity. Participation was voluntary. The researchers were available to explain and assist with any queries to prevent data contamination. Following the introduction of the study, the objectives of the study were explained, followed by the issuance of the questionnaire and information letter. The data extracted included the answers to all questions posed in the questionnaire and the demographic information.

### Data analysis

Data was entered into the RedCap database and analysed using the statistics programme STATA® version 16.1. Summary statistics were reported using frequencies and percentages for categorical responses and means with standard deviations for continuous measurements. Categorical data were presented as frequencies and percentages. Data describing anaesthetic practice were presented as either mean ( $\pm$  standard deviation) if normally distributed or median (interquartile range) if not normally distributed. Continuous variables were compared using analysis of variance (ANOVA). The Kruskal Wallis' test was used if the continuous variable was not normally distributed. The association between categorical variables was evaluated using Pearson's chi-square test. A 95% confidence interval was used. The statistically significant level was set at a p-value  $< 0.05$ .

### Ethical consideration

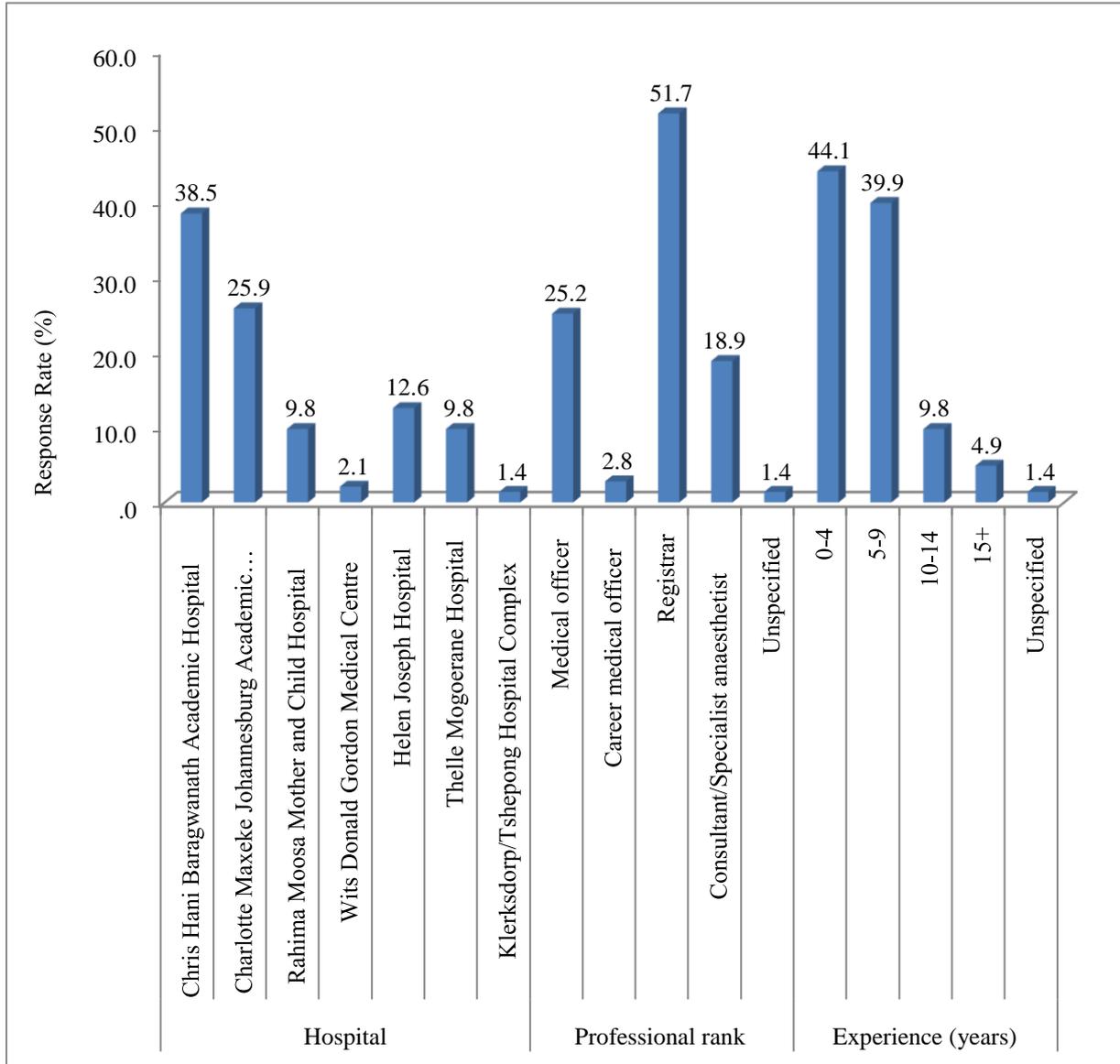
Ethics approval was obtained from the Human Ethics Clearance Committee (Medical) and the Graduate Studies Committee of the University of the Witwatersrand. Anonymity and confidentiality of participants were ensured by use of an anonymised questionnaire completed electronically using the RedCap link. Data was securely stored electronically on a password-protected RedCap account, and access was limited to the researchers.

### Validity and reliability

To ensure face and content validity, this questionnaire was reviewed by three senior anaesthetists who conduct OFA regularly in the department. The researcher was always available to answer any questions and prevent data contamination. Participant anonymity was guaranteed as no personal identifying information was acquired. Every tenth data entry point on the spreadsheet was checked for accuracy. Data will be made available upon request.

### Results

Several statistical tests were employed to establish the mathematical relationships between the variables studied and assess their significance. Figure 1.1 shows that in terms of professional rank, registrars had greater knowledge of OFA, followed by medical officers and specialist anaesthetists.



**Figure 1: Participants' knowledge of OFA, affiliated hospital, professional rank, and years of experience.**

Figure 2 shows that a significant number of participants reported not having any knowledge of OFA protocols ( $p = 0.030$ ). Additionally, more participants indicated that their hospital did not have a formal OFA protocol ( $p < 0.001$ ).

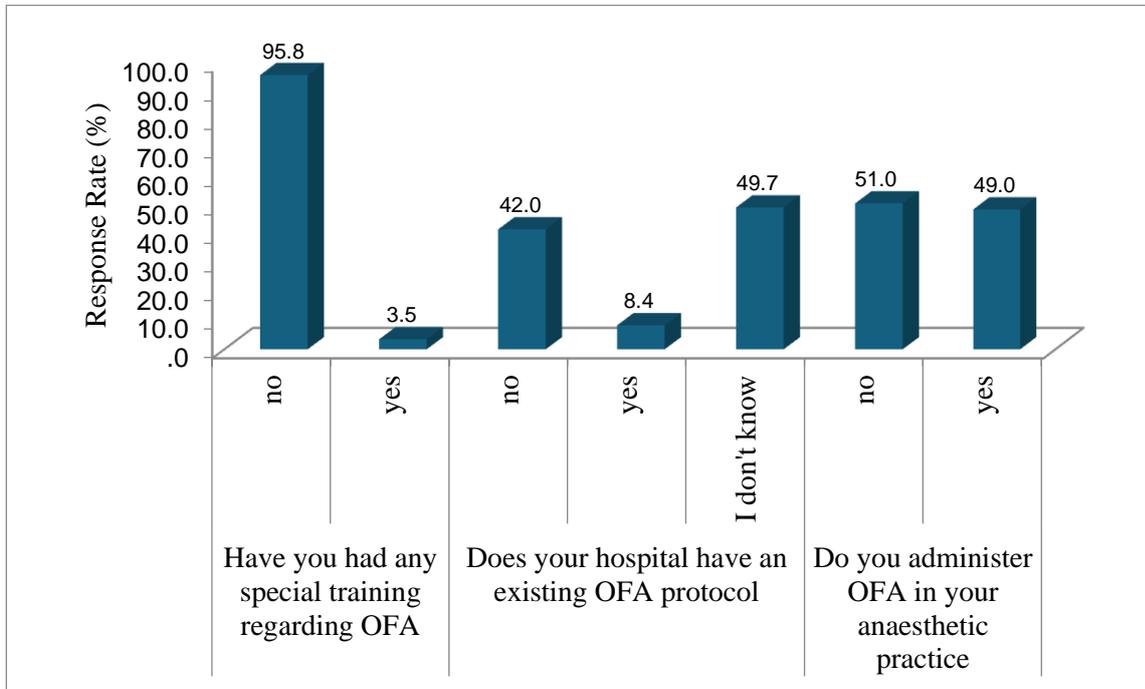


Figure 2: The Practice of OFA

Figure 3 illustrates a statistically significant preference for specific agents used in the practice of OFA, with p-values less than 0.01. The most commonly selected agents by respondents included Ketamine (70.6%), Dexmedetomidine (72%), Sevoflurane (62.2%), Magnesium sulphate (61.5%), and Lignocaine (66.4%).

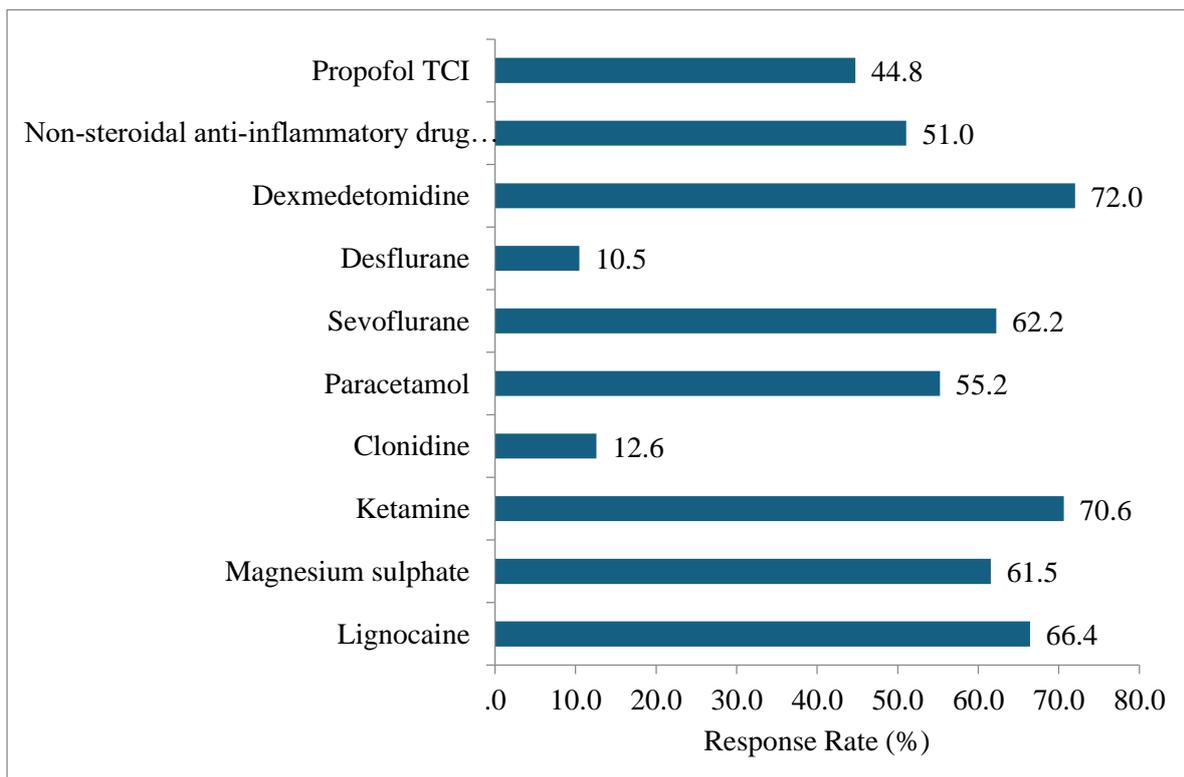


Figure 4 illustrates the reasons for a shift in perception regarding the liberal use of opioids, highlighting the major factors contributing to the reduction in their use. The primary reasons cited by more than 79% of participants include the potential for respiratory complications associated with opioid use and the need to

promote the practice of ERAS. The same figure also demonstrates that participants in the study were aware of the potential for opioids to result in tolerance, as well as immune suppression in oncology patients, which poses additional challenges to their usage.

**Figure 4: Arguments against the liberal use of opioids.**

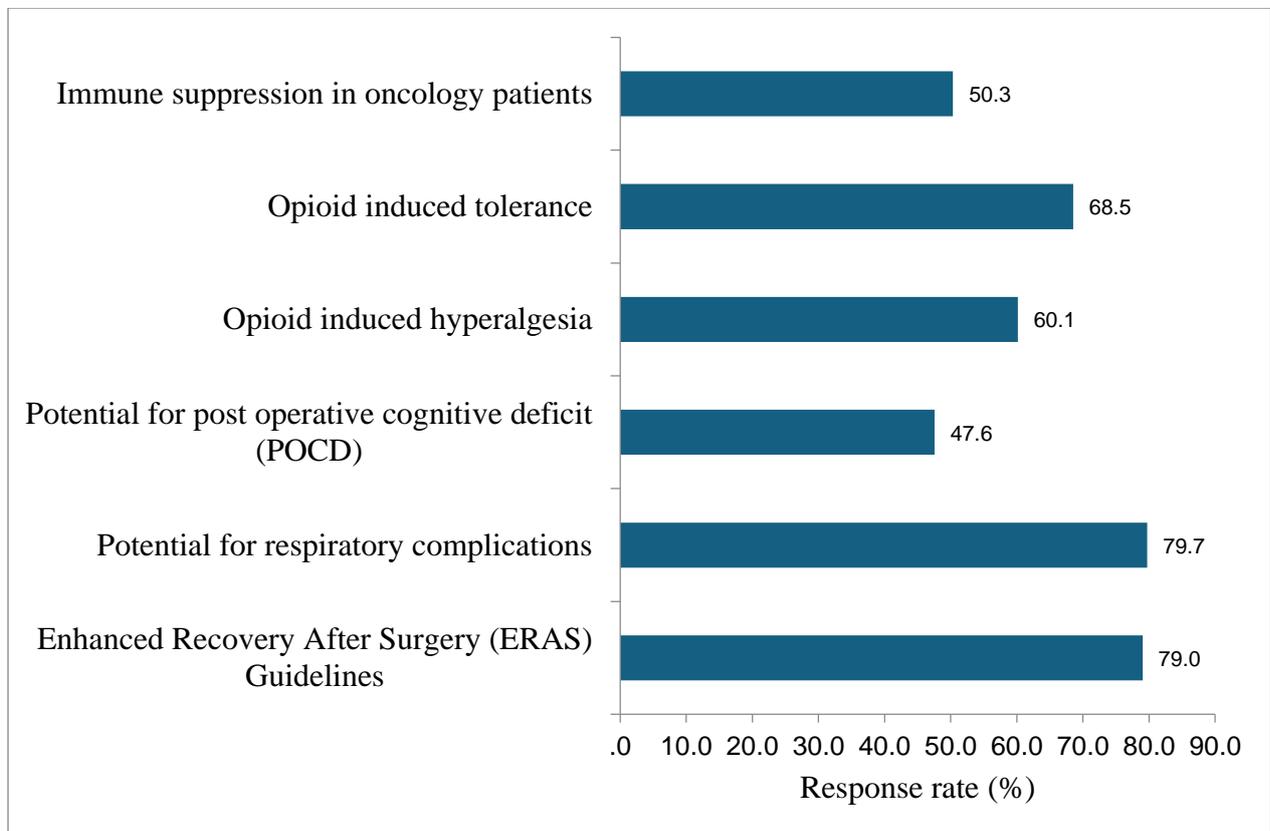
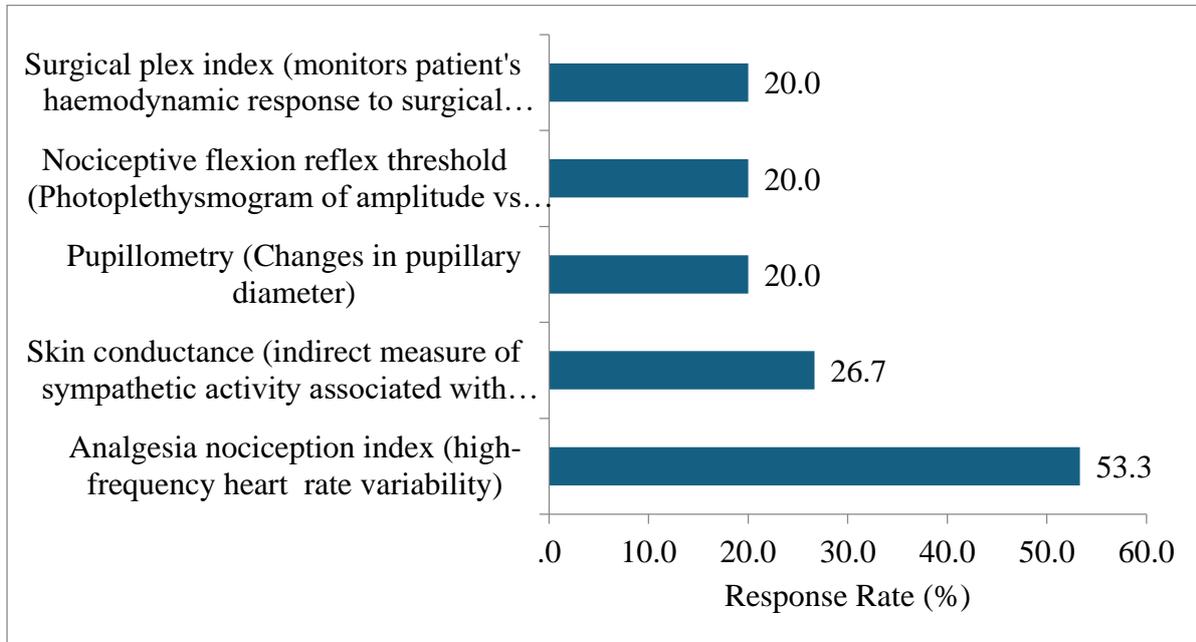


Figure 5 illustrates participants' experience with the use of nociceptive monitors in OFA. 53% of respondents reported having experience with the Analgesia Nociception Index (high-frequency heart rate variability), while only 27% reported the usage of skin conductance monitors. Statistical analysis using binomial

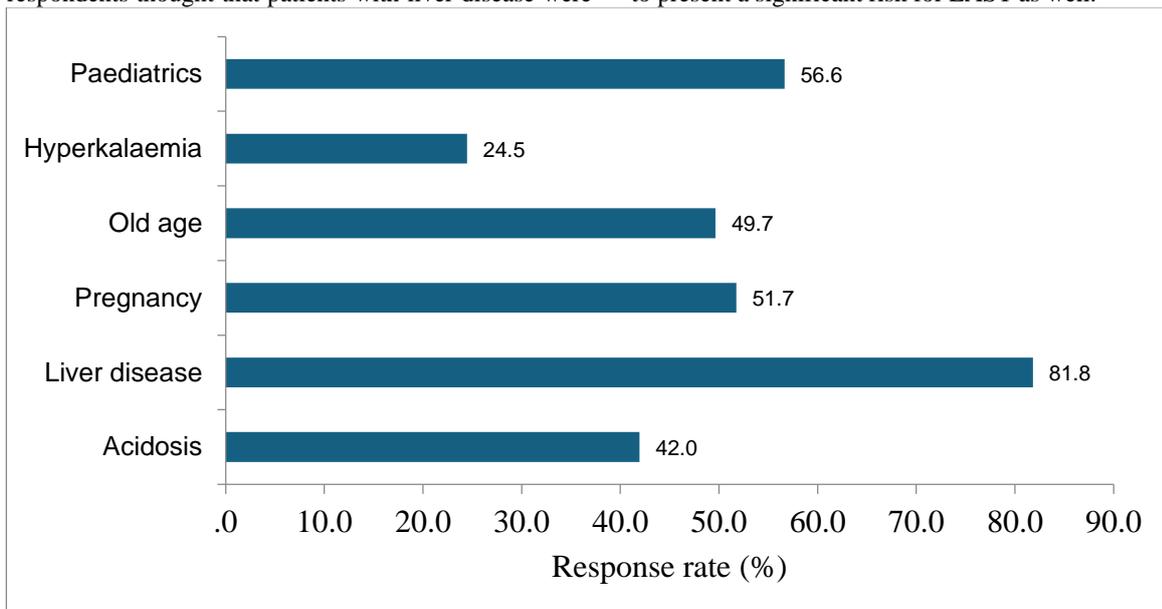
tests indicated that the experience rates for pupillometry (20%), nociceptive flexion reflex threshold (20%), and surgical plexus index (20%) were significantly lower than expected; these were statistically significant (p value 0.035).



**Figure 5 Anaesthetists' experience with nociceptive monitors.**

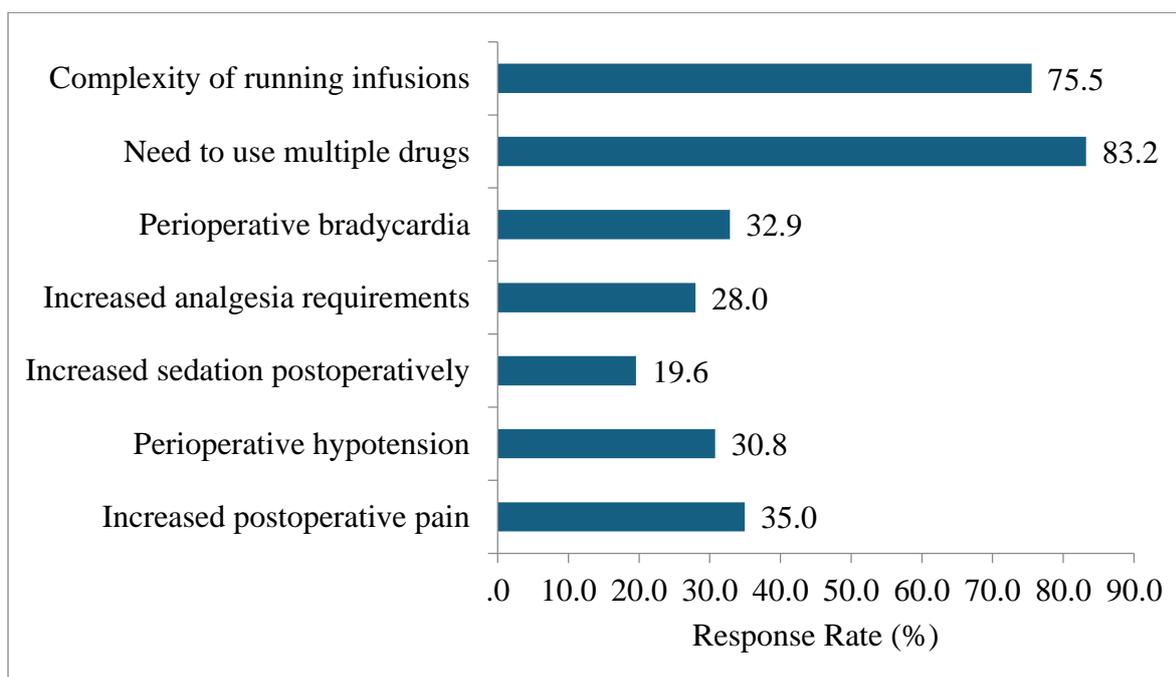
Due to the heavy emphasis on the use of local anaesthetics as part of their role in OFA, Local Anaesthetic Systemic Toxicity (LAST) is identified as a material risk. Figure 6 demonstrates that 81.8% of respondents thought that patients with liver disease were

the highest risk for LAST. Additionally, 56.6% of respondents thought that the paediatric population and 51.7% that the pregnant population was an at-risk group for LAST. Advanced age and acidosis were also reported to present a significant risk for LAST as well.



**Figure 6 Patient factors that increase the risk of Local Anaesthetic Systemic Toxicity (LAST)**

The main reported disadvantages of OFA, as described by participants, as seen in Figure.7, were that 83.2% of participants felt that OFA protocols required the administration of multiple drugs, and 75.5% felt that running infusions can be quite challenging.



**Figure 7: The Challenges in the Practice of OFA.**

## Discussion

This study demonstrated a significant association between professional rank and knowledge of OFA. The superior knowledge of OFA observed among registrars in our study can be attributed to factors related to training and professional development. Registrars are exposed to structured specialist training programmes which mandate involvement in research activities, journal clubs, and CPD sessions that support contemporary anaesthetic practice. Newton et al. <sup>(10)</sup> emphasized that structured postgraduate education significantly enhances knowledge and skills in evolving medical fields.

## OFA Practice Patterns

According to the European Society of Anaesthesiology and Intensive Care (ESAIC), anaesthetists are more likely to practice OFA if there are clearly described guidelines to follow <sup>11</sup>. Figure 2 shows a significant finding regarding the lack of established OFA protocols in our academic hospitals, which is important as it

creates an inconsistent clinical environment for encouraging the practice of OFA.

## Pharmacological Agents in OFA

Figure 3 illustrates statistically significant preferences for specific agents used in OFA. Propofol (81.1%) and Lignocaine (69.9%) emerged as the most commonly used induction agents, both statistically significant findings ( $p < 0.001$ ), affirming their central role in OFA. Additionally, Dexmedetomidine was reported to be important in the maintenance of OFA ( $p < 0.001$ ). Midazolam and Clonidine were notably underutilised, despite their known synergistic benefits in OFA protocols <sup>12</sup>. These findings suggest a lack of training and challenges related to drug availability.

## The benefits of OFA

A significant number of respondents reported the main advantages of OFA to be a decreased incidence of respiratory depression and PONV. According to Olausson et al. <sup>(13)</sup>, the use of OFA decreased PONV by 78%; however, there was no evidence of a decreased

incidence of respiratory depression. Additionally, OFA aligns with ERAS protocols to facilitate earlier mobilisation, improve patient comfort, accelerate recovery, and potentially shorten hospital stays<sup>13</sup>.

### **Nociceptive Monitors**

According to reported data (Figure 5), 53.3% of respondents cited the Analgesia Nociception Index (based on high-frequency heart rate variability) as the most utilized nociceptive monitor in clinical practice. Other nociceptive monitors had notably lower response rates, ranging between 20.0% and 26.7%. Reasons for these findings include lack of training, resource limitations, cost, and technical complexity. Additionally, a chi-square goodness-of-fit test conducted on participants' perceptions of nociceptive monitor utility showed that a significant number did not know whether nociceptive monitors provided sufficient clinical benefit ( $\chi^2 (2) = 43.729, p < 0.001$ ). These results suggest considerable uncertainty among anaesthetists regarding the value of nociceptive monitoring, and currently, there is no study supporting the routine use of nociceptive monitors in OFA.

### **Risk Factors for LAST**

Local anaesthetics are significant adjuncts in OFA, emphasizing the need for anaesthetists to be knowledgeable regarding the rare, though potentially lethal, complication of LAST. Figure 6 illustrates participants' knowledge regarding the risk factors of LAST.

- Liver dysfunction: Impaired hepatic metabolism can lead to accumulation of local anaesthetic agents, increasing systemic toxicity risk<sup>14</sup>.
- Paediatric patients: Immaturity of hepatic metabolic pathways, altered pharmacokinetics, larger volume of distribution, and reduced plasma protein binding increase the free drug fraction<sup>15</sup>.
- Pregnant patients: Increased cardiac output, reduced alpha-1 acid glycoprotein, and enhanced neural sensitivity elevate risk<sup>16</sup>.
- Older age (49.7%): Age-related reductions in hepatic blood flow, decreased metabolic capacity, and increased sensitivity to local anaesthetics heighten risk<sup>17</sup>.
- Acidosis (42%): Acidosis increases the free fraction of local anaesthetic in plasma and reduces the efficacy of lipid rescue therapy<sup>18</sup>.
- Hyperkalemia: Although not directly causing LAST, hyperkalemia can exacerbate cardiac toxicity when LAST occurs, promoting conduction abnormalities and arrhythmias<sup>19</sup>.

According to Weibel et al.<sup>20</sup>, the toxic dose of intravenous Lignocaine run as an infusion as per OFA protocols is 1.5–2.5 mg/kg/h. The study revealed a significant number of respondents knew this dose ( $p$ -value  $< 0.001$ ). This indicates a good level of pharmacological knowledge among participants, which may mitigate the risk of LAST in OFA.

### **Limitations of the study**

Convenience sampling provides simplicity of sampling and data collection in a shorter duration of time; however, it leaves this study vulnerable to selection bias. The study was only conducted on Wits anaesthesia providers, and findings may not necessarily be extrapolated to other anaesthetic departments in South Africa.

### **Conclusion**

The safe practice of OFA is a skill that presents a steep learning curve. OFA is challenging in centres where there are resource constraints, as not all the drugs may be readily available, and anaesthetists may not be familiar with their use in this paradigm. The study showed that a significant percentage of anaesthetists in our centre did not have any OFA training, and this was a key factor limiting their practice of OFA.

### **Recommendations**

Training programmes that mandate involvement in research activities, journal clubs, and CPD events focused on OFA. Hospital-specific OFA protocols based on resources available would encourage the practice of OFA.

### **Author's contributions**

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**SWAG:** conceptualised the study design, wrote the study protocol, collected data, analysed the data, and wrote the first draft of the article.

**AIM:** provided research support and assisted with study design, data analysis, data presentation, and article drafting.

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### Conflict of interest

The authors declare no conflict of interest.

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### List of Acronyms

CPD: Continuous professional development  
HREC: Human research ethics committee  
ESAIC: European Society of Anaesthesiology and Intensive Care  
ERAS: Enhanced recovery after surgery  
LAST: Local anaesthetic systemic toxicity  
OFA: Opioid free anaesthesia  
OPCAB: off-pump coronary artery bypass graft  
POCD: Postoperative cognitive decline  
PONV: Post-Operative Nausea and Vomiting  
REDCap: Research electronic data capture

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