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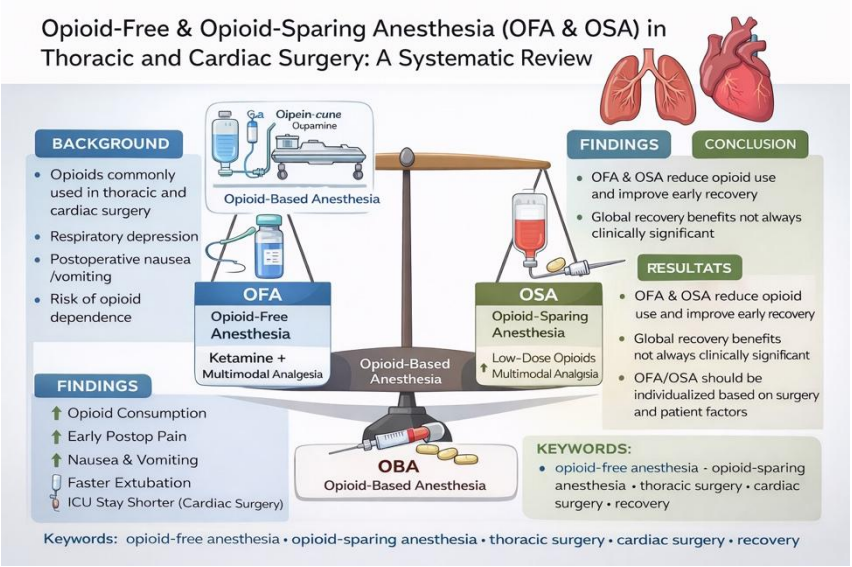
Comparison of Opioid-Free Anesthesia and Opioid-Based Anesthesia on Intraoperative Quality and Postoperative Recovery of Thoracic and Cardiac Surgery: Systematic Review and Meta-analysis

Gunawan Leonard Sitorus, Vera Muharrami

Correspondence Email : gunawanleonard.gl@gmail.com

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Graphical Abstract



Abstract

Background Opioids are component main anesthesia in surgery thoracic and cardiac , however its use relate with various effect side postoperatively . Opioid-Free Anesthesia (OFA) and Opioid-Sparing Anesthesia (OSA) approaches were developed For reduce risk said , but its effectiveness to quality recovery post-operative Still need reviewed more carry on . **Objective :** Evaluate effectiveness and safety of OFA and OSA compared to Opioid-Based Anesthesia (OBA) against quality intraoperative and recovery post- operative surgery thoracic and cardiac . **Methods:** Review systematic done through PubMed and Google Scholar searches on publication until 2024. Included studies includes clinical trials randomized and studies observational study evaluating OFA /OSA in surgery thoracic and cardiac . Data analyzed in a way narrative-critical . **Results:** OFA and OSA in consistent lower opioid consumption and pain post-operative early as well as reduce incidence nausea and vomiting post-operatively . During surgery heart , OFA is related with time extubation and longer ICU stay short . In VATS,

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OFA increases Quality of Recovery- 40 score statistics , however Not yet meaningful in a way Clinical . **Conclusion:** OFA and OSA are safe and feasible anesthetic strategies in surgery . thoracic and cardiac , with benefit main focus on recovery early . Approach This should implemented individually according to type surgery and characteristics patient .

Keywords : Opioid-free anesthesia ; opioid-sparing anesthesia ; thoracic surgery; cardiac surgery; post-operative recovery.

Abstract

Background Opioids are the main component of anesthesia in thoracic and cardiac surgery, however their use is related to various side effects postoperatively. Opioid-Free Anesthesia (OFA) and Opioid-Sparing Anesthesia (OSA) approaches were developed For reducing risk said , but its effectiveness to quality post-operative recovery Still need to be reviewed more carry on . **Objective:** Evaluate effectiveness and safety of OFA and OSA compared to Opioid-Based Anesthesia (OBA) against quality of intraoperative and post-operative recovery in thoracic and cardiac surgery. **Methods:** Systematic review conducted through PubMed and Google Scholar searches on publications until 2024. Included studies include randomized clinical trials and observational studies evaluating OFA /OSA in thoracic and cardiac surgery. Data analyzed in a narrative- critical way. **Results:** OFA and OSA in consistent lower opioid consumption and early post-operative pain as well as reduced incidence of nausea and vomiting post- operatively. During heart surgery, OFA is related to extubation time and longer ICU stay . In VATS, OFA increases Quality of Recovery- 40 score statistics , but Not yet meaningful in a Clinical way . **Conclusion:** OFA and OSA are safe and feasible anesthetic strategies in surgery. thoracic and cardiac, with the benefit of main focus on early recovery. This approach should be implemented individually according to type of surgery and patient characteristics.

Keywords : Opioid -free anesthesia ; opioid-sparing anesthesia ; thoracic surgery; cardiac surgery; post-operative recovery.

1. Introduction

difficult history For determine When and where did this opium poppy plant grow ? first cultivated . At first plant This planted For taken the seeds before man find method prepare Mecon from leaves and fruit plant said . Opium originate from Greek, namely Opos which means latex said . Latex the is fluid that comes out from capsule unripe seeds ripe when sliced .

Although there is difficulty in interpreting ancient writings and archaeological data , depicting use of opium in ancient times still can arranged . In a general agreed that nation Sumerians , who inhabited the present region known as Iraq , has cultivate

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poppy plants and isolate opium from them capsule the seeds at the end millennium third SM. They called opium " gil *"* , which means joy , and the poppy plant as " *hul gil* ", or plant joy . It seems poppy then spread from Sumerian to the whole old world (6).

There is evidence to suggest that Since 3000 BC, the opium poppy, Papaver somniferum, has been cultivated For material active . However , new after morphine isolated from opium in 1806 by Sertürner , modern opioid pharmacology is truly born . In 1847 , the formula chemistry morphine concluded and this , plus with invention needle injection in 1853 , causing use clinical more morphine precise and extensive (5). In the beginning , opium may used as substance euphoria in religious rituals , it is drunk or inhaled from heated container (7) .

Confession wide will need management pain and spikes opioid prescription at the end 18th century and early the 19th century led to global opioid epidemic . This movement , which is also supported by the industry pharmaceuticals , resulting in disturbance opioid use and a number of big death patient consequence opioid overdose .[1] This opioid crisis push community medical and expert anesthesia For review back management strategy pain that reduces or remove opioid use and remains give reliever effective pain (1).

Opioids have become an integral part of practice anesthesia . In historically , in ancient India , surgery done by experts surgery great , Susruta , around 600 BC with aid of opium, wine , and Indian marijuana (a type of plants). Science surgery called " salya -tantra" (salya : broken parts) from child arrows and weapons sharp others ; tantra: maneuver) (2). Far then , in 1805 , a pharmacist brilliant , Friedrich Wilhelm Adam Serturner, isolated crystal morphine from thick poppy seed extract (3). The era of synthetic opioids began in the 1950s, and in 1962 the use of synthetic opioids first , fentanyl , in anesthesia explained in Belgium . Since that , opioids have become essential components in anesthesia balanced (4).

Classification

The most well-known P. Soniverum There are 4 natural alkaloids that can isolated from him namely : Morphine, Codeine , Papaverine , and Thebaine. After isolation morphine by Sertürner as component active from opium poppy, manipulation chemistry

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simple from basic opioid alkaloids This start produce various useful semi - synthetic opioids in treatment clinical (agent like diamorphine , dihydrocodeine , buprenorphine , nalbuphine, naloxone , and oxycodone).

During the 20th century , a number of synthetic opioids were also produced . Good in a way on purpose and No intentionally . Compound synthetic This can shared become four group chemistry : derivatives morphine (levorphanol , butorphanol), derivatives diphenylheptane (methadone , propoxyphene), derivatives benzomorphans (pentazocine , phenazocine) and derivatives phenylpiperidines (pethidine , alfentanil, fentanyl , sufentanil and remifentanil).

Opioids can also classified according to its effect on opioid receptors . With method this , opioids can considered as agonists, partial agonists , and antagonists . Agonists interact with receptors For produce response maximum from receptors said (analgesia after giving morphine is for example).

On the contrary , the antagonist bound with receptors but No produce response functional , while at the same time prevent agonist binding with receptors (naloxone). Partial agonist bound with receptors but only cause response functional partial let go from amount the drug given (buprenorphine).

Table 1. Classification of opioids based on the synthesis process

Natural Opioids	synthetic Opioids	Synthetic Opioids
Morphine	Diamorphine (Heroin)	Pethidine
Codeine	Dihydromorphone	Fentanyl
Tebaine	Buprenorphine	Methadone
Papaverine	Oxycodone	Alfentanil
		Remifentanil
		Tapentadol

Table 2. Evolution naming opioid receptors to standard international moment This

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Before Cloning	After Cloning	IUPHAR 1996	IUPHAR 2000 (Official)
δ (delta)	BANG	OP1	HUBCAP
κ (kappa)	KOR	OP2	HEAD
μ (mu)	MOR	OP3	MOP

The Future of Opioids in Management Anesthesia

After develop butyrophenones (haloperidol and droperidol), Paul Janssen diverted his attention to synthetic opioids . He take example from previous German researchers who focused on meperidine and the ring piperidine , which he said important in induce analgesia. Understand approach chemistry For build ring piperidine important For understand opioid problem today This .

Whereas structure molecule morphine based on the ring phenanthrene and found in plants , meperidine based on the ring distant piperidine more simple . With objective find more compounds late than morphine , Janssen researchers replaced group methyl bonded to the N atom in the molecule meperidine with benzene ring (9).

They Then adding C=O to ring new benzene placed and found that matter That increase potential analgesic . Changing C=O to C-OH is increasingly increase analgesic potential . Compound This named phenoperidine and is fentanyl precursor . Modification more carry on from molecule the produce synthesis sufentanil , alfentanil, and carfentanil (9). Every derivation change potency , onset, duration , and termination effect

Neurobiology addicted is field intensive research on animals rodents . Taught mice For pressing lever For consume drugs addictive (heroin, cocaine , amphetamines) will start show behavior addictive , such as case in point humans who are addicted , and not will Eat or sleep , show activation excessive lever , and shows characteristic features behavior addicted others (10). When the drug the removed from environment , related pleasures with giving drug the No forgotten , but still intact during months , which resulted reactivation and desire as response to signal addicted or stress .

In the perioperative period , analgesia is determinant main anesthesia balanced and

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usually achieved with giving opioid agents because good tolerance and maintaining stability hemodynamics . But perioperative opioid administration does not free risk . Opioids are associated with effect threatening side soul like depression breathing , nausea , and vomiting post surgery , hyperalgesia due to opioids (11). Some study find correlation between post-op opioid administration operations , development painful chronic , and opioid addiction (12).

So that opioid administration should be reduced or avoided as much as possible maybe . There is increasing evidence Lots show that Opioid Free Anesthesia (OFA). However surgery thorax is distant fields more challenges that are associated with level pain and complications more lungs tall compared to with operation other .

2. Materials and Methods Study

Study This use approach studies literature critical narrative review with analysis historical and evidential clinical about use Opioid Free anesthesia and anesthesia with Opioids in Thoracotomy . Search literature done in a way systematically on PubMed and Google Scholar databases for publication speaking English and Indonesian published since 1903 to 2024. Keywords used covering *opioid-free* , *opioid-sparing* , *regional anesthesia* , *block* , *local anesthetic* , *ketamine* , *dexmedetomidine* , *bupivacaine* , *ropivacaine* , *lidocaine* , *thoracic surgery* , *lobectomy* , *bilobectomy* , *segmentectomy* , and *pneumonectomy* , both in a way single and in various combination using Boolean operators. Criteria inclusion covers report case study observational , clinical trials , reviews systematic , and publication historical which discusses safety , effectiveness , and complications use Opioid Free anesthesia and anesthesia with Opioids in Thoracotomy . Articles that are not relevant , duplicate , or No provide clear clinical data issued from analysis .

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3. Results

No	Year	Researchers	Title Research / Journal	Types of Anesthesia	Anesthesia Techniques – Analgesia and Surgery	Number of Samples	Conclusion
1	2025	Vasileia Nyktari, et al.	A Perioperative Opioid-Sparing Anesthesia - Analgesia Strategy Feasible in Open Thoracotomies? Findings from a Retrospective Matched Cohort Study	**OSA-A (Opioid-Sparing Anesthesia – Analgesia)**	Anesthesia general without regional or epidural block . • Lobectomy 39 patients • Segmentectomy 14 patients • Pneumonectomy 3 patients • Other Open Thoracotomy 4 patients	60 patients	Postoperative pain more low , opioid requirements in the PACU are higher a little , PACU (Post-Anaesthesia Care Unit) which is more short , intestinal motility is greater fast , nausea and vomiting more a little ; pain chronicle No different meaningful
				OBA-A (Opioid-Based Anesthesia – Analgesia)	Anesthesia general without regional or epidural block Anesthesia general without regional or epidural block .	40 patients	More pain high , opioid needs are greater big in PACU (Post-Anaesthesia Care Unit), being in the PACU longer , bowel recovery is slower slow , nausea and vomiting more often

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					• Lobectomy 23 patients • Segmentectomy 12 patients • Other Open Thoracotomy 5 patients		
2	**2019**	**Guinot et al.**	**Effect of opioid-free anesthesia on the post-operative period in cardiac**	**Opioid-Free Anesthesia (OFA)**	Anesthesia general without regional or epidural block . Anesthesia general multimodal non- opioid (lidocaine , dexamethasone , ketamine , propofol); surgery heart with cardiopulmonary bypass • Valvular surgery 20 patients • Coronary artery bypass grafting (CABG) 11 patients	55 patients	Lower consumption morphine post-operative , accelerate time extubation , shortening the length of ICU stay , and reducing number major complication compared to OA.

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			surgery: a retrospective matched case-control study		• Combined surgery (CABG + valve disease) 21 patients • Ascending aortic replacement in 1 patient • Left ventricular assist device (LVAD) implantation in 2 patients		
				Opioid-Based Anesthesia (OBA)	Anesthesia general without regional or epidural block . Anesthesia general multimodal non- opioid (lidocaine , dexamethasone , ketamine , propofol); surgery heart with cardiopulmonary bypass • Valvular surgery 22 patients	55 Patients	Consumption morphine post-operative more high , extubation more slower , longer ICU stays , and more major complications often compared to OFA.

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					• Coronary artery bypass grafting (CABG) 9 patients • Combined surgery (CABG + valve disease) 21 patients • Ascending aortic replacement in 1 patient • Left ventricular assist device (LVAD) implantation in 2 patients		

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3	**2024**	**Choi *et al***	**Opioid-Free Using Ketamine versus Opioid-Sparing Anesthesia during the Intraoperative Period in Video-Assisted Thoracoscopic Surgery: A Randomized Controlled Trial**	**Opioid-Free Anesthesia (OFA)**	**Operation** : **Video-Assisted Thoracoscopic Surgery (VATS)** • Lobectomy • Segmentectomy lungs	45 patients	- **OFA with ketamine** give significant improvement in QoR-40 in a way statistics , however No meaningful in a way clinical compared to OSA. - OFA more Good in : • Lower painful beginning postoperative (0–4 hours) • Reducing PONV • Reduce postoperative shivering - OFA causes time wake up and extubate longer , but : • Hemodynamics stable • No intraoperative awareness was found .
				Opioid Sparing Anesthesia (OSA)	**Operation** : **Video-Assisted Thoracoscopic Surgery (VATS)** • Lobectomy • Pulmonary segmentectomy	46 patients	

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Review This analyze literature that evaluates use of Opioid-Free Anesthesia (OFA) and Opioid-Sparing Anesthesia (OSA) compared with Opioid-Based Anesthesia (OBA) in surgery thoracic and cardiac . Included studies includes clinical trials randomized study cohort retrospective with matched cohort, as well as studies case-control retrospective , with range year publication from 2019 to 2025. Types of surgery analyzed includes :

- Surgery thorax open (lobectomy , segmentectomy , pneumonectomy , and thoracotomy) other),
- Surgery minimally invasive thoracic using Video-Assisted Thoracoscopic Surgery (VATS),
- Surgery heart with use of cardiopulmonary bypass, including surgery valves , CABG, combined CABG– valve , and procedures complex other .

Total population patient in studies main analyzed amount to more of 300 patients , with relative distribution balanced between OFA/OSA group and OBA group .

OFA and OSA approaches analyzed generally use anesthesia general multimodal, with elimination or intraoperative opioid restrictions . The most common agents used in OFA regimen includes :

- Ketamine dose subanesthetic (bolus and infusion),
- Lidocaine intravenously ,
- Dexamethasone,
- Propofol as agent hypnotic main .

Most of the studies No use regional or epidural blocks , especially during surgery heart and thorax open , so that observed effects especially reflect contribution regimen pharmacological systemic . In the VATS study , several protocol combining OFA with non-opioid multimodal analgesia and thoracic paravertebral block , as appropriate principles of Enhanced Recovery After Surgery (ERAS).

Group OBA or OSA comparator in general using potent opioids such as remifentanil or fentanyl during period intraoperatively , with postoperative analgesia opioid -based according to protocol standard .

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In a way consistent , the studies analyzed show that OFA and OSA approaches are related with :

- Decline intensity painful post-operative early , especially in the first 0–4 hours ,
- Decline opioid needs in the PACU and the phase beginning maintenance ,
- Reduction in total postoperative opioid consumption compared to OBA.

In surgery thorax open , OSA-A is associated with decline opioid needs in the PACU as well as recovery better gastrointestinal function fast . In surgery heart , OFA in significant lower consumption morphine post-operative compared to anesthesia opioid- based .

However thus , in some parts study , differences pain in the 24–48 hour postoperative period become No meaningful , showing that OFA's main advantages located in phase recovery beginning .

Quality recovery post-operative assessed use instrument standardized such as the Quality of Recovery-40 (QoR-40) in the VATS study . The results showed that :

- The QoR-40 score in the OFA group was higher tall in a way statistics compared to OSA,
- However difference the No achieve the minimum clinically important difference (MCID).

QoR-40 domain analysis shows that OFA's main advantages originate from :

- Pain domain ,
- Domain of comfort physical , while other domains such as independence physical and support psychological relatively similar between group .

Findings This show that OFA increases aspect specific recovery , however Not yet Of course increase perception global patient recovery in a way clinical meaningful .

In surgery heart , OFA is related with :

- Longer extubation time short ,

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- Duration more ICU care short ,
- Decline number major postoperative complications .

On the other hand , in surgery minimally invasive thoracic , OFA- based ketamine reported cause :

- Short wake- up time and extubation longer , but without impact negative to stability hemodynamics or safety patient .

Difference This show that OFA effect on recovery respiration and extubation nature contextual , depending type operations , agents used , and protocols anesthesia companion .

In a way In general , OFA and OSA indicate profile good safety . The studies analyzed report :

- Decline incidence nausea and vomiting postoperative (PONV),
- Decline postoperative shivering incident ,
- Not found improvement intraoperative awareness events or psychosis postoperative use ketamine dose subanesthetic .

Stability hemodynamics intraoperatively in the OFA group in general comparable with OBA, although a number of protocol need adjustment agent vasoactive For maintain pressure blood and pulse heart .

4. Conclusion

Review systematic narrative This show that Opioid-Free Anesthesia (OFA) and Opioid-Sparing Anesthesia (OSA) is approach safe and appropriate anesthesia applied to surgery thoracic and cardiac approach This in a way consistent relate with decline postoperative opioid consumption and improvement external recovery early , especially painful post-operative onset , PONV, and duration maintenance intensive .

However , the increase quality recovery globally , as measured with instrument standardized like QoR-40, not yet in a way consistent reach meaning clinically significant . This is show that OFA benefits more nature specific to the external certain

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compared to transformation comprehensive to experience recovery patient .

Effectiveness and impact The clinical course of OFA is greatly influenced by the type of surgery , protocol multimodal anesthesia is used , as well characteristics population patient . Therefore that , OFA should viewed as part of individualized anesthesia strategies , no as a universal approach that replaces opioids completely .

Study prospective scale big with clinical trial design randomized , analysis subgroup based on type operations , as well as evaluation external term long Still required For determine optimal role of OFA and OSA in practice modern anesthesia , especially in surgery thoracic and cardiac .

5. Conflict Interest

Researchers state No there is conflict interest

6. Funding Sources

Researchers This No accept funding special from any institution.

7. Agreement Ethics

Study This is a systematic review/meta-analysis that uses secondary data from publication scientific that has available and not involving subject man in a way directly , so that No need agreement ethics from Committee Ethics Health Research . Protocol study This has registered with PROSPERO with registration number ID 1302913

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