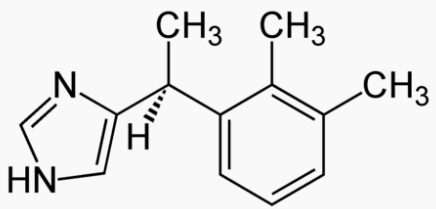
# Dexdor ® pour l'OFA (Opioid Free Anesthesia) en chirurgie orthopédique

**Dexmédétomidine**




Dr Clément Chassery

Médi POLE Garonne
Clinique du sport Médico-Chirurgicale

Tolos' IADE
Association pour la Formation des IADE et des IDE de SSPI



GIPSE
L'excellence en formation santé

# Déclaration de conflit d'intérêt


Aucun

# Plan

- Pourquoi faire de l'OFA ?
- Comment faire de l'OFA ?
- Place du Dexdor ®
- Dexdor ®: quelles précautions ?
- Notre expérience

# Evolution des pratiques de l'AG

AG balancée

Standardisée
Dose -poids

Hypnotique

Opioide de synthèse

Curare

# Evolution des pratiques de l'AG

AG balancée

AG

Standardisée
Dose -poids

multimodale

Hypnotique

Dexa Kétamine

Opioide de synthèse

ALR

Curare

# Evolution des pratiques de l'AG

Opioid-sparing A

multimodale

Hypnotique

Dexa Kétamine

▼ Opioide

▲ ALR

Curare

Alpha 2 agonistes Sulfate Mg2+ LidoC IV

# Evolution des pratiques de l'AG

Opioid-sparing A

Opioid Free A

multimodale

Hypnotique

Dexa Kétamine

▼ Opioide

∅

▲ ALR

Curare

Alpha 2 agonistes Sulfate Mg2+ LidoC IV

# Intérêt des opioïdes

| Pour | Contre |
| --- | --- |
| Contrôle de la nociception | Dépression respiratoire |
| ↓ dose hypnotique | RAU-Constipation |
| Stabilité hémodynamique | Hyperalgésie |

*Kiyatkin EA. Neuropharmacology 2019*

*Verhamme KM. Drug Saf 2008*

*Farmer AD. Lancet Gastroenterol Hepatol 2018*

*Fletcher D.Br J Anaesth 2014; 112:991-1004*

# ↓ les doses d'opioïdes ?

*British Journal of Anaesthesia* **112** (6): 991–1004 (2014)
doi:10.1093/bja/aeu137

BJA

**Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis**

D. Fletcher[1,2,3*] and V. Martinez[1,2,3]

+ 18 mg EMO/ 24 h

↑ douleur repos 24 h

› Eur J Anaesthesiol. 2019 Nov;36(11):871-880. doi: 10.1097/EJA.0000000000001081.

**Association between intra-operative fentanyl dosing and postoperative nausea/vomiting and pain: A prospective cohort study**

Eckhard Mauermann, Damian Clamer, Wilhelm Ruppen, Oliver Bandschapp

↑ dose Fentanyl® per op

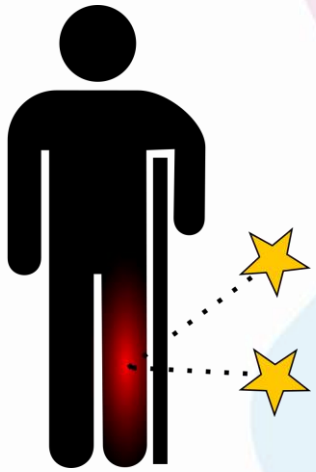
↑ douleur à 24h

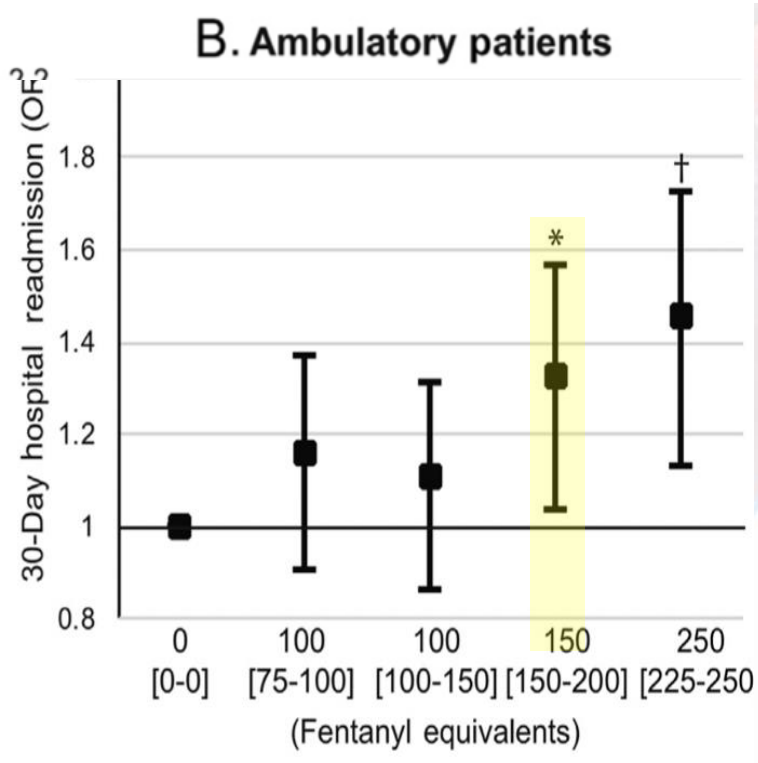
↑ NVPO

## Association between intraoperative opioid administration and 30-day readmission: a pre-specified analysis of registry data from a healthcare network in New England

D. R. Long[1], A. L. Lihn[1,2], S. Friedrich[1], F. T. Scheffenbichler[1], K. C. Safavi[1], S. M. Burns[1], J. C. Schneider[3], S. D. Grabitz[1], T. T. Houle[1] and M. Eikermann[4,5,*]

*British Journal of Anaesthesia*, 120 (5): 1090—1102 (2018)





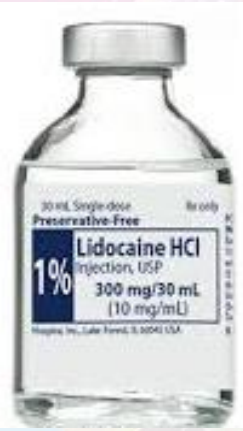

Variabilité des doses suivant l'anesthésiste

# Comment faire de l'OFA ?

AL

ALR








8-10mg IV

<0.5mg/kg IV

# Indications du Dexdor ®

## Réanimation

Sédation en USI (Unité de Soins Intensifs) chez l'adulte nécessitant un état de sédation pas plus profond que celui permettant une réponse à un stimulus verbal (correspondant à un score de 0 à -3 sur l'échelle de vigilance-agitation de Richmond (RASS)).

VIDAL

## Anesthésie

Sédation de patients adultes non intubés avant et/ou pendant les actes à visée diagnostique ou chirurgicale nécessitant une sédation, telle qu'une sédation procédurale/vigile.

# Action du Dexdor ®

## Agoniste Récepteurs α2

| dci | Clonidine |
|---|---|
| | Catapressan® |
| Distribution centrale | 20 min |
| Afinité Récepteurs α2/ α1 | 200/1 |
| ½ vie d'élimination | 12-16 h |
| Métabolisme hépatique | |
| Effet secondaire | HypoTension |

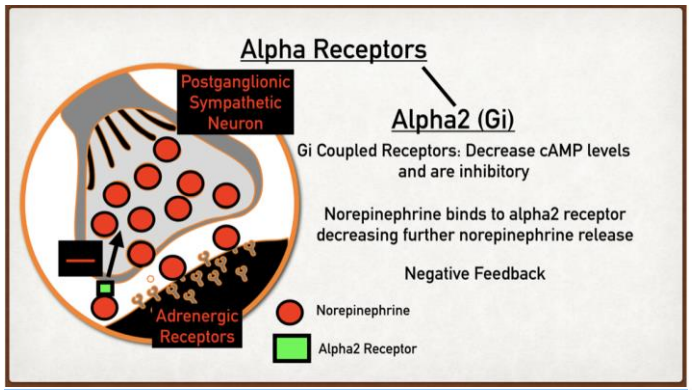
| Anesthésie |
|---|
| B: 0.5- 1 µg/kgIVL<br>+/- 0.2-1 µg/kg/h<br>(Max 1.4 µg/kg/h) |

Tarif 2019 : 27 euros HT l'ampoule

Tarif 2020 : 12 euros HT l'ampoule

Tarif 2021 : 5 euros HT l'ampoule

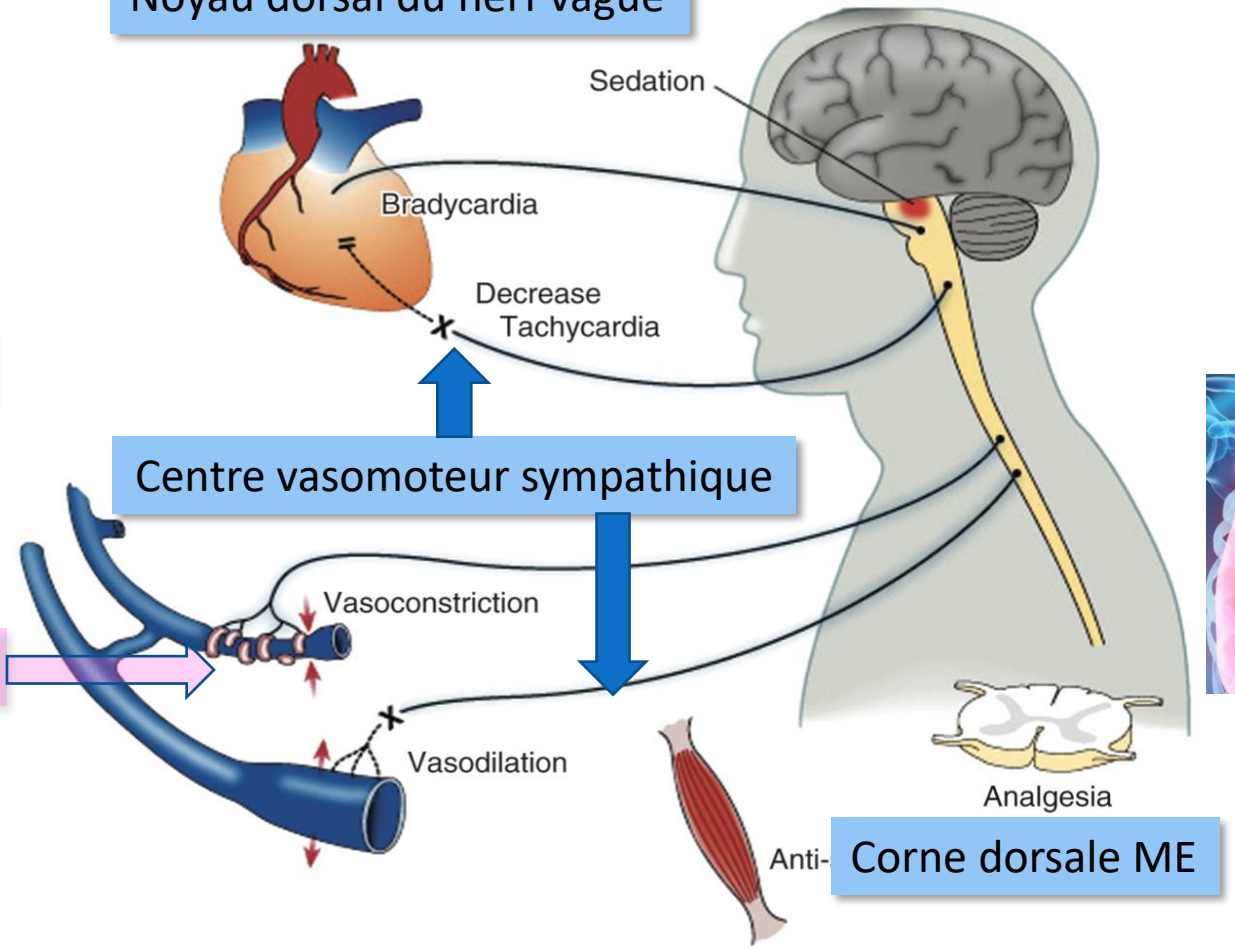
Tarif 2022 : 2,4 euros HT l'ampoule




Rα2 Pré synaptiques Centraux

Noyau dorsal du nerf vague

Locus coeruleus




Rα2 Post synaptiques périphériques

Muscles lisses

Corne dorsale ME

# Contre-indications du Dexdor ®

- Bloc cardiaque avancé
  - Bloc sinusal
  - BAV2-3
- Hypotension non contrôlée
- Pathologies cérébrovasculaires aigues

- Bradycardie
- Risque d'instabilité hémodynamique
- Insuffisance hépatique sévère
- Grossesse
- Allaitement

*Review*

# Opioid-Free Anesthesia Benefit–Risk Balance: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

**Arthur Salomé [1], Hakim Harkouk [1,2], Dominique Fletcher [1,2] and Valeria Martinez [1,2,*]**

- 33 études
  - 2209 patients
- Chir diverses
- Opiacés vs OFA
  - 22 études avec Dexdor®

| | OFA | |
|---|---|---|
| EVA 2h | - 0.76/100 | Significatif |
| EVA 24 h | NS | |
| EVA 48h | NS | |
| Conso morphine 2 h | -1.61 mg | Significatif |
| Conso morphine 24h | -1.73 mg | Significatif |
| Conso morphine 48h | -3.14 mg | Significatif |
| Nausée à24h | RR 0.55 | Significatif |
| Vomissement SSPI | RR 0.34 | |
| Douleur à 3 mois | NS | |

Grande hétérogénéité

## Opioid-free anaesthesia for anterior total hip replacement under general anaesthesia: the Observational Prospective Study of Opiate-free Anesthesia for Anterior Total Hip Replacement trial

Brendan Urvoy[1], Christophe Aveline[2,*], Nicolas Belot[3], Charles Catier[3] and Hélène Beloeil[1]

doi: 10.1016/j.bja.2021.01.001
Advance Access Publication Date: 3 February 2021

Etude observationnelle

PTH voie antérieure sous AG

AG: Propofol puis Sévo / Dexa/ Keta/ Cisatracurium

Analgésie: Paracétamol + Kétop + nefopam + A locale

Stratégie OFA (dexdor) vs OBA (suf) 0.4 µg/kg

**OFA**

↓EVA

↓ Morphine 24h

↓ désaturation SSPI

↑ délai extubation

↑Ephédrine

# Dexdor ®: quelles précautions ?

ANESTHESIOLOGY

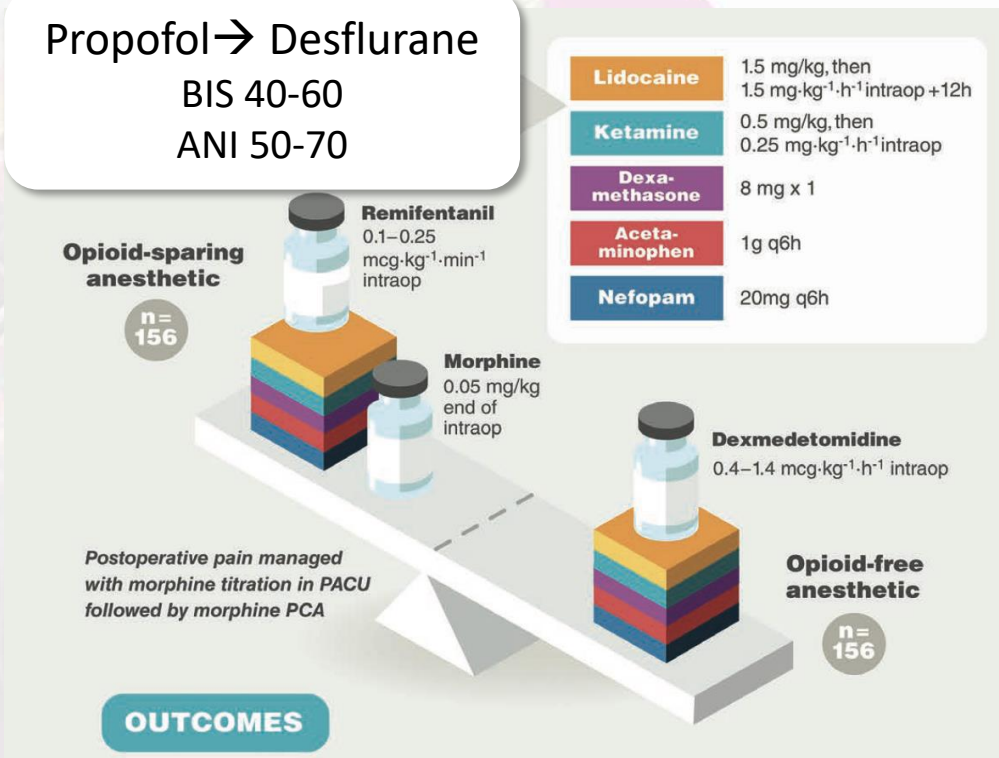
**Balanced Opioid-free Anesthesia with Dexmedetomidine *versus* Balanced Anesthesia with Remifentanil for Major or Intermediate Noncardiac Surgery**

The Postoperative and Opioid-free Anesthesia (POFA) Randomized Clinical Trial

Helene Beloeil, M.D., Ph.D., Matthias Garot, M.D., Gilles Lebuffe, M.D., Ph.D., Alexandre Gerbaud, M.D., Julien Bila, M.D., Philippe Cuvillon, M.D., Ph.D., Elisabeth Dubout, M.D., Sebastien Oger, M.D., Julien Nadaud, M.D., Antoine Becret, M.D., Nicolas Coullier, M.D., Sylvain Lecoeur, M.D., Julie Fayon, M.D., Thomas Godet, M.D., Michel Mazerolles, M.D., Fouad Atallah, M.D., Stephanie Sigaut, M.D., Pierre-Marie Choinier, M.D., Karim Asehnoune, M.D., Ph.D., Antoine Roquilly, M.D., Ph.D., Gerald Chanques, M.D., Ph.D., Maxime Esvan, Ms.C., Emmanuel Futier, M.D., Ph.D., Bruno Laviolle, M.D., Ph.D., for the POFA Study Group* and the SFAR Research Network†

*ANESTHESIOLOGY 2021; 134:541–51*

Propofol→ Desflurane
BIS 40-60
ANI 50-70



# Dexdor ® :quelles précautions ?

| | RemiF | DexM | |
|---|---|---|---|
| Hypoxie | 61 % | 72% | P=0.03 |
| Morphine 48 h | 11 mg | 6 mg | p<0.05 |
| Incidence NVPO | 37 % | 24 % | P<0.05 |
| Durée en SSPI | 1h53 | 2h28 | P=0.01 |
| Bradycardie | 9 % | 19 % | P=0.009 |

## Hypoxie

Def: SpO2< 95% sans apport d'O2

## Sédation SSPI

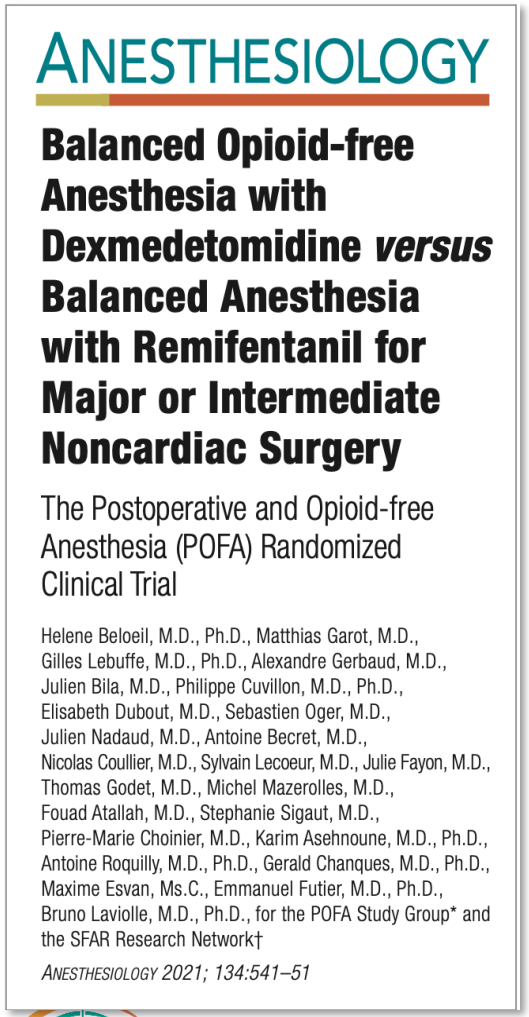
Dose élevée Dexdor 1.2 µg/kg/h

Pas d'arrêt anticipé

Association Lidoc IV et Keta

5 Bradycardies sévères

# 5 Bradycardies sévères



ANESTHESIOLOGY

**Balanced Opioid-free Anesthesia with Dexmedetomidine *versus* Balanced Anesthesia with Remifentanil for Major or Intermediate Noncardiac Surgery**

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*ANESTHESIOLOGY 2021; 134:541–51*

**Traitement**

4 injections d'atropine

1 injection d'adrénaline

→1 report de chirurgie

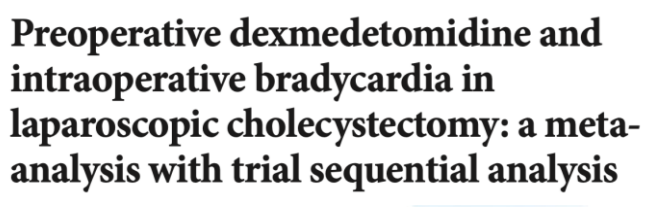
**Causes**

1 surdosage dexdor ®

4 laparoscopies

KJA

Korean Journal of Anesthesiology



**Preoperative dexmedetomidine and intraoperative bradycardia in laparoscopic cholecystectomy: a meta-analysis with trial sequential analysis**

**Clinical Research Article**

Korean J Anesthesiol 2022;75(3):245-254
https://doi.org/10.4097/kja.21359
pISSN 2005-6419 • eISSN 2005-7563

**Bradyc x 2.81**

Médi POLE Garonne
Clinique du sport Médico-Chirurgicale

# Prothèse totale de hanche

**Perop**

**AG avec ML**

TIVA propofol (2-3mg/kg+ IVSE) + Keta 0.4mg/kg + Dexa 10mg

Paracétamol 1gr + Kétoprofène 100mg

Nefopam 20mg IV

Infiltration : Ropiv 0.2% 100 ml

**Postop**

PCT 1gr/6h + ibu 400mg/8h

+/- oxynorm 10 mg PO

**OSA**

Sufenta 10 µg

+/-5 µg

**OFA**

Dexdor® 1 µg. $Kg^{-1}$ IVL 15min

+/-0.4 µg. Kg

# PTH Ambu sous AG :étude OFATHA

*à paraitre au BJA*

Consommation opioïde 24h IDEM

Consommation opioïde FAIBLE

Score de douleur FAIBLE

Durée SSPI identique

Bonne tolérance hémodynamique

Peu d'échec d'ambulatoire

**Table 2.** Pain management outcomes in the opioid-sparing anaesthesia (OSA) and opioid-free anaesthesia (OFA) groups.

| | OSA group (n=40) | OFA group (n=40) | | P value * |
|---|---|---|---|---|
| Bradycardia, n (%) | 6 (15) | 9 (23) | 1.6 (0.5 to 5.2) | 0.4 |
| Atropine injection, n (%) | 4 (10) | 7 (18) | 1.9 (0.5 to 7.1) | 0.3 |
| Atropine, mg | 0.5 (0.5-0.9) | 1.0 (0.5-1.0) | - | 0.2 |
| Hypotension, n (%) | 19 (48) † | 13 (33) | 0.5 (0.2 to 1.3) | 0.2 |
| Phenylephrine or Ephedrine injection, n (%) | 14 (35) | 8 (20) | 0.5 (0.2 to 1.3) | 0.1 |
| Phenylephrine, mg | 0.1 (0.1-0.2) | 0.1 (0.1-0.1) | - | - |
| Ephedrine, mg | 12.0 (9.0-16.5) | 6.0 (6.0-15.0) | - | 0.3 |
| Prolonged hospitalization, n (%) | 4 (10) | 0 (0) | 0.1 (0.0 to 1.9) | 0.1 |
| Bleeding, n (%) | 0 (0) | 1 (3) | 3.1 (0.1 to 77.9) | 1.0 |
| Laryngospasm, n (%) | 1 (3) | 0 (0) | 0.3 (0.0 to 8.2) | 1.0 |
| Nausea or vomiting, n (%) | 3 (8) | 1 (3) | 0.3 (0.0 to 3.2) | 0.6 |
| Voiding difficulties, n (%) | 0 (0) | 2 (5) | 5.3 (0.2 to 113.2) | 0.5 |
| Drowsiness, n (%) | 1 (3) | 1 (3) | 1.0 (0.1 to 16.6) | 1.0 |
| Dizziness, n (%) | 8 (20) | 2 (5) | 0.2 (0.0 to 1.1) | **<0.05** |

# PTG sous ALR et Sédation

**Préop**

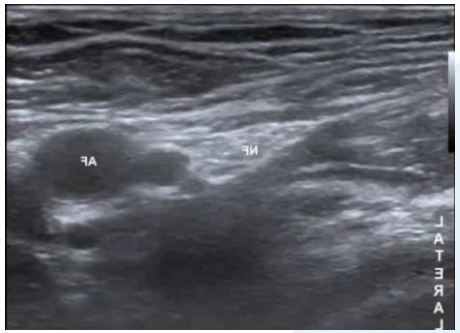
PTG sous Quadribloc (Ropi 0.32% 60m

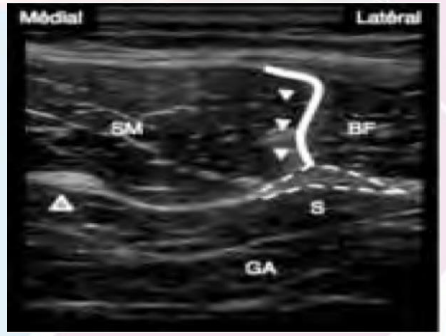
-Bloc Fémoral

-Bloc Sciatique

-Bloc Obturateur

-Bloc CLC






*Marty P. Br J Anaesth. 2022 Sep;129(3):427-434*
*Chassery C et al. Reg Anesth Pain Med 2020;0:1-7*

**Perop**

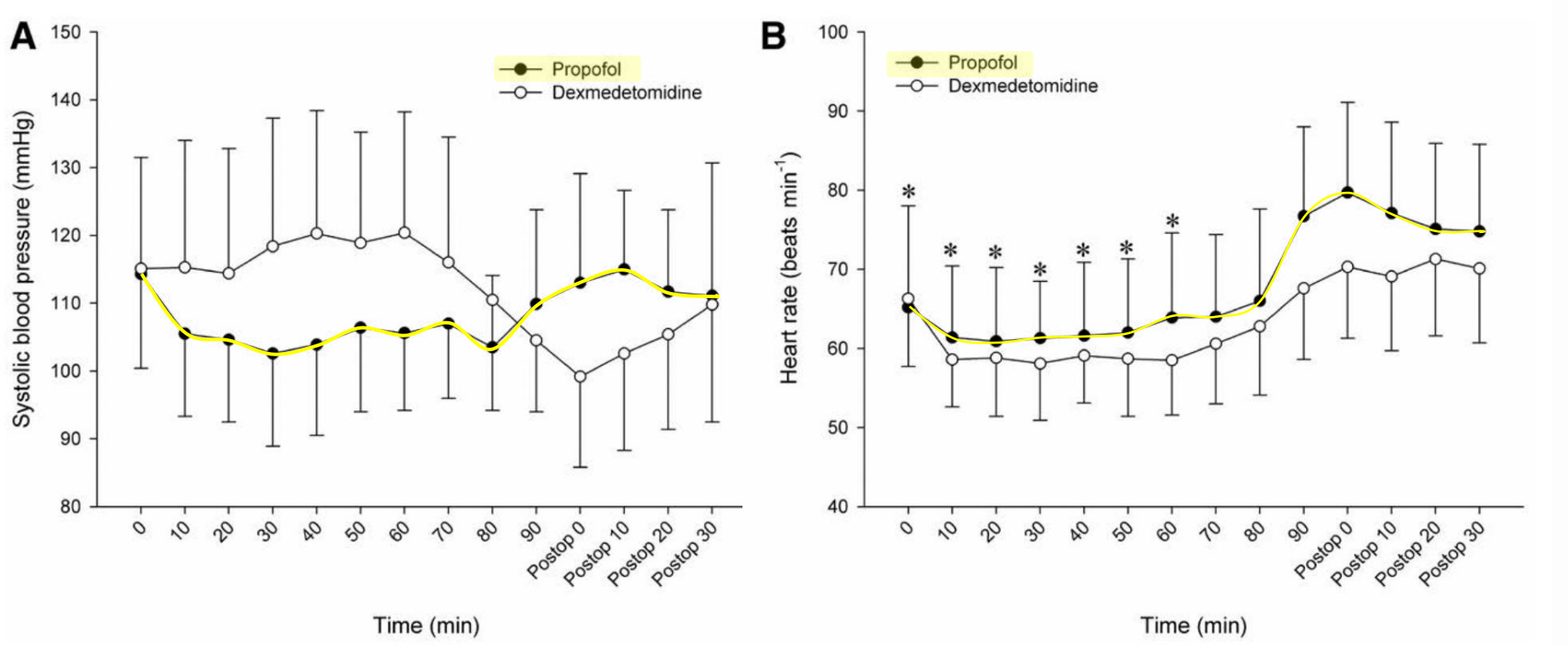
Sédation per opératoire

Kétamine 0.3mg/kg IV

+/- Propofol 5-10 cc/h IVSE

# PTG sous RA et Sédation

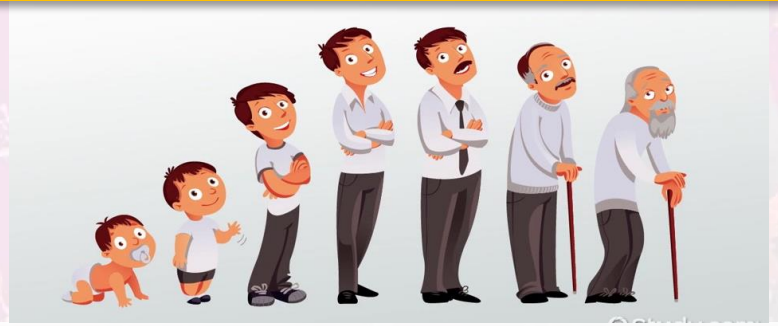
## Profil hémodynamique




*Shin, Hyun-Jung. Anesth Analg. 2018 Apr 5*

# PTG sous ALR + Sédation

## Adapter la dose à l'âge



ED95 Dexdor® IV pour sédation légère

- 18-45 ans: 1,21 µg/kg
- 45-65 ans: 0.84 µg/kg
- >65 ans: 0.54 µg/kg

*Bo Xu. Anesth Analg. 2017*

# OFA avec Dexdor ®en orthopédie

Stabilité hémodynamique

Analgésie post op efficace

Chirurgie réglée

non hémorragique

Patient sélectionnées

Dose Dexdor ® adaptée

Meta-Analysis > J Clin Anesth. 2020 Oct:65:109849. doi: 10.1016/j.jclinane.2020.109849.
Epub 2020 May 8.

# Intravenous administration of dexmedetomidine and quality of recovery after elective surgery in adult patients: A meta-analysis of randomized controlled trials

Mengrong Miao [1], Yuehua Xu [1], Bing Li [1], Enqiang Chang [1], Liyuan Zhang [1], Jiaqiang Zhang [2]

## Abstract

**Study objective:** To evaluate the efficacy and safety of pre- and perioperative intravenous administration of dexmedetomidine for enhancing quality of recovery (as measured by 40-item quality of recovery questionnaire (QoR-40), ranged from 40 to 200) after surgery.

**Design:** Meta-analysis.

**Setting:** Adult patients undergoing elective surgery.

**Intervention:** Intravenous administration of dexmedetomidine during pre- and perioperative period.

**Measurements:** The primary outcome was quality of recovery after surgery. The secondary outcome was the incidence of dexmedetomidine-related adverse events.

**Main results:** Moderate to low quality evidence suggested that dexmedetomidine (DEX) increased the quality of recovery after surgery (WMD, weighted mean difference 15.71, 95% CI, confidence interval 0.43 to 31.00; 428 participants; 5 RCTs; low quality evidence), decreased the incidence of postoperative nauseas or vomiting (RR, risk ratio 0.60, 95% CI 0.44 to 0.83; 404 participants; 6 RCTs; moderate quality evidence; RR 0.32, 95% CI 0.19 to 0.55; 356 participants; 5 RCTs; moderate quality evidence) without increased risk of bradycardia (RR: 1.78, 95% CI 0.78 to 4.02; 275 participants; 4 RCTs; moderate quality evidence), dizziness (RR 0.78, 95% CI 0.31 to 2.00; 183 participants; 3 RCTs; moderate quality evidence), pruritus (RR 1.32, 95% CI 0.39 to 4.44; 186 participants; 3 RCTs; moderate quality evidence), hypotension requiring an intervention (RR: 1.48, 95% CI, 0.68 to 3.23; 254 participants; 3 RCTs; moderate quality evidence) and longer length of hospital stay (WMD: -0.75 days, 95% CI -1.95 to 0.44; 246 participants; 3 RCTs; low quality evidence) in early postoperative period.

**Conclusions:** Dexmedetomidine as an anesthetic adjuvant to general anesthesia was associated with an enhanced quality of recovery (15.71; far more than a clinically significant improvement of 6.3) without increased risk of adverse events in the early postoperative period (moderate to low quality evidence). Further large sample and high quality RCTs are needed to confirm the current findings.

# The effect of opioid-free anesthesia protocol on the early quality of recovery after major surgery (SOFA trial): study protocol for a prospective, monocentric, randomized, single-blinded trial

Maxime Léger[1,2*], Solène Pessiot-Royer[1], Tristan Perrault[1], Elsa Parot-Schinkel[3], Fabienne Costerousse[1], Emmanuel Rineau[1] and Sigismond Lasocki[1]

**Abstract**

**Background:** Since the 2000s, opioid-free anesthesia (OFA) protocols have been spreading worldwide in anesthesia daily practice. These protocols avoid using opioid drugs during anesthesia to prevent short- and long-term opioid side effects while ensuring adequate analgesic control and optimizing postoperative recovery. Proofs of the effect of OFA protocol on optimizing postoperative recovery are still scarce. The study aims to compare the effects of an OFA protocol versus standard anesthesia protocol on the early quality of postoperative recovery (QoR) from major surgeries.

**Methods:** The SOFA trial is a prospective, randomized, parallel, single-blind, monocentric study. Patients ($n$ = 140) scheduled for major plastic, visceral, urologic, gynecologic, or ear, nose, and throat (ENT) surgeries will be allocated to one of the two groups. The study group (OFA group) will receive a combination of clonidine, magnesium sulfate, ketamine, and lidocaine. The control group will receive a standard anesthesia protocol based on opioid use. Both groups will receive others standard practices for general anesthesia and perioperative care. The primary outcome measure is the QoR-15 value assessed at 24 h after surgery. Postoperative data such as pain intensity, the incidence of postoperative complication, and opioid consumption will be recorded. We will also collect adverse events that may be related to the anesthetic protocol. Three months after surgery, the incidence of chronic pain and the quality of life will be evaluated by phone interview.

**Discussion:** This will be the first study powered to evaluate the effect of OFA versus a standard anesthesia protocol using opioids on global postoperative recovery after a wide range of major surgeries. The SOFA trial will also provide findings concerning the OFA impact on chronic pain incidence and long-term patient quality of life.

| Opioid free anesthesia protocol | Standard anesthesia protocol |
|---|---|
| **Before surgery** | |
| – **CLONIDINE** continuous infusion: start at 50 µg/h, with anesthetic monitoring, and adapt to hemodynamic stability with a maximum infusion rate of 150 µg/h. If patient's weight <50kg, maximum infusion rate of 100µg/h<br>– **Locoregional anesthesia** if needed, but without opioids | – **Locoregional anesthesia** if needed, with or without opioids |
| **Anesthesia induction** | |
| – **Antibiotic prophylaxis** if indicated<br>– **Hypnotic drugs**: left at the discretion of the anesthesiologist<br>– **NO OPIOIDS**<br>– **CLONIDINE** continuous infusion on same infusion rate, adapt to hemodynamic stability<br>– **MAGNESIUM sulfate**: 40 mg/kg, *diluted in 100ml of NaCl 0.9%, IV infusion* Maximum dose: 4 g<br>– **LIDOCAINE**: 1.5 mg/kg in 10 minutes (continuous infusion) *(if loco-regional anesthesia, this dose is not administered)*<br>– **KETAMINE**: 0.5 mg/kg as a bolus (or 0.25 mg/kg if instable coronary disease or instable cardiac failure or pulmonary arterial hypertension)<br>– **Neuromuscular blocking agents** (anesthesiologist's discretion)<br>– **Nausea and vomiting management** | – **Antibiotic prophylaxis** if indicated<br>– **Hypnotic drugs:** left at the discretion of the anesthesiologist<br>– **Opioids:**<br>○ **Sufentanil** 0.1-0.3 µg/kg IV<br>Or<br>○ **Remifentanil** via target-controlled infusion,<br>○ target: 3-6 ng/mL<br>– **KETAMINE:** left at the discretion of the anesthesiologist in charge<br>0.15 mg/kg IV, can be repeated every 45 min-1hour<br>– **Neuromuscular blocking agents** (anesthesiologist's discretion)<br>– **Nausea and vomiting management** |
| **Intra-operative anesthesia** | |
| – **Hypnotic drugs**: left at the discretion of the anesthesiologist<br>○ Inhalation anesthetic agents: Desflurane or Sevoflurane with a MAC (Mean Alveolar Concentration) objective of 1-1.5 MAC<br>OR<br>○ Propofol via target-controlled infusion, target at 3-6 µg/mL<br>– **No Opioids**<br>– **CLONIDINE** on continuous infusion on same infusion rate, adapt to hemodynamic stability<br>– **KETAMINE** 0.2 mg/kg/h on continuous infusion, stopped 30 minutes before end of surgery<br>– **LIDOCAINE** on continuous infusion: 1.5 mg/kg/h, continued up to 1h after the surgery<br>– **Pain management** according to the service protocol:<br>○ **ACETAMINOPHEN** 1 g IV<br>○ +/- **NEFOPAM** 20 mg IV<br>○ +/- **KETOPROFEN** 50 to 100 mg IV<br>○ **No opioids**<br>– **Neuromuscular blocking agents** left at the discretion of anesthesiologist | – **Hypnotic drugs**: left at the discretion of the anesthesiologist<br>○ Inhalation anesthetic agents: Desflurane or Sevoflurane with a MAC (Mean Alveolar Concentration) objective of 1-1.5 MAC<br>OR<br>○ Propofol via target-controlled infusion, target at 3-6 µg/mL<br>– **Opioids**<br>○ **Sufentanil** 0.1-0.3 µg/kg with bolus intervals left at the discretion of the anesthesiologist in charge<br>OR<br>○ **Remifentanil** via target-controlled infusion, target: 3-6ng/mL<br>– **Pain management** according to the service protocol:<br>○ **ACETAMINOPHEN** 1 g IV<br>○ +/- **NEFOPAM** 20 mg IV<br>○ +/- **KETOPROFEN** 50 to 100 mg IV<br>○ +/- **OXYCODONE** or **MORPHINE** 1-5 mg IV<br>– **Neuromuscular blocking agents** left at the discretion of anesthesiologist |
| **Postanesthesia care unit (PACU)** | |
| – **LIDOCAINE** on continuous infusion: 1.5 mg/kg/h, continued up to 1 hour after the surgery in the PACU<br>– **Pain management** (opioids can be used if necessary)<br>– **Nausea and vomiting management** | – **Pain management** (opioids can be used if necessary)<br>– **Nausea and vomiting management** |

**Fig. 1** Detailed interventional protocols in the opioid-free anesthesia group (OFA group) and in the standard anesthesia group (English translation from our French procedures). IV, intravenous; PACU, postanesthesia care unit

# Alpha Receptors

## Alpha1 (Gq)

(Smooth Muscle Contraction)

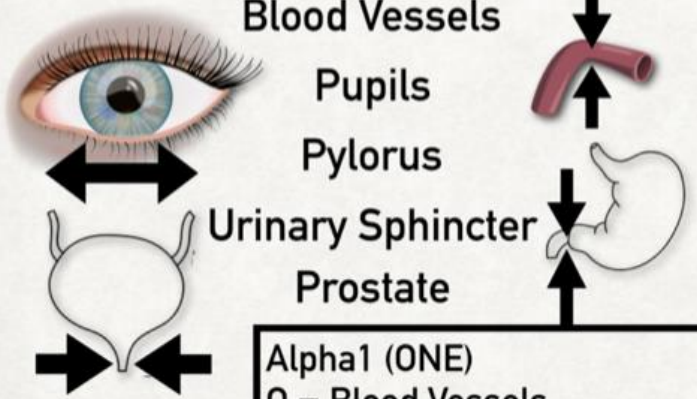
Blood Vessels

Pupils

Pylorus

Urinary Sphincter

Prostate



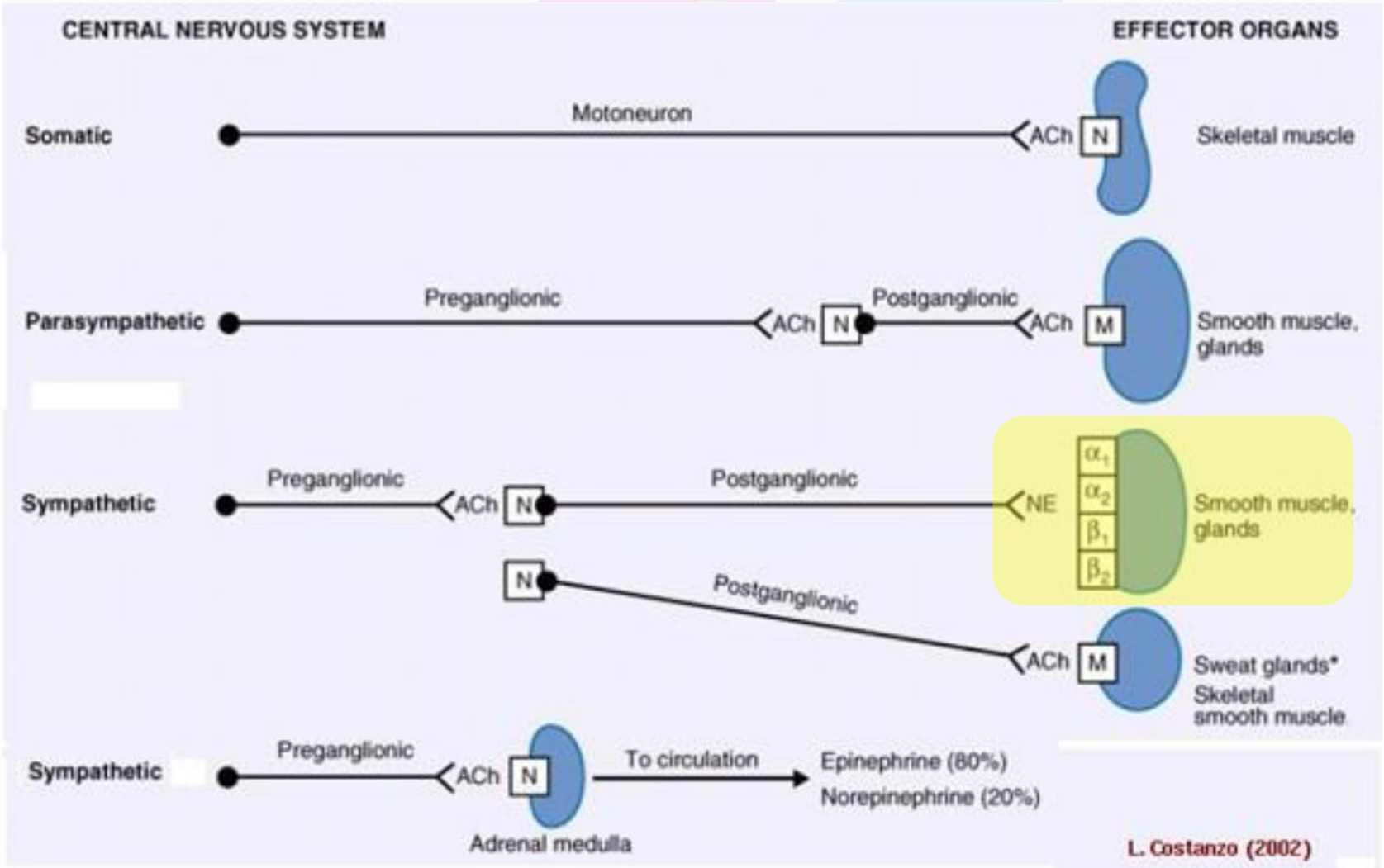
Alpha1 (ONE)
O = Blood Vessels
N = Neck of bladder, prostate, stomach
E = Eye

## Alpha2 (Gi)

(Inhibitory)

Presynaptic Nerve Terminals


Alpha2 (Two)
TWO = Terminal Weaning Off


CENTRAL NERVOUS SYSTEM
EFFECTOR ORGANS
Somatic
Motoneuron
ACh
N
Skeletal muscle
Parasympathetic
Preganglionic
ACh
N
Postganglionic
ACh
M
Smooth muscle, glands
Sympathetic
Preganglionic
ACh
N
Postganglionic
NE
α1
α2
β1
β2
Smooth muscle, glands
N
Postganglionic
ACh
M
Sweat glands*
Skeletal smooth muscle
Sympathetic
Preganglionic
ACh
N
To circulation
Epinephrine (80%)
Norepinephrine (20%)
Adrenal medulla
L. Costanzo (2002)