Jan P Mulier

Sint jan Brugge, Belgium

2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Anaesthesia dosage and opioid administration in morbidly obese patients

British Journal of Anaesthesia **108** (2): 193–201 (2012)
doi:10.1093/bja/aer458

BJA

Postoperative intravenous morphine titration

F. Aubrun[1]*, J.-X. Mazoit[2] and B. Riou[3]

[1] Department of Anesthesiology and Critical Care, Université Claude Bernard Lyon 1, Groupe Hospitalier Nord, Hôpital de la Croix Rousse, Lyon, France
[2] Department of Anesthesiology and Critical Care, Université Paris-Sud 11, Hôpital Bicêtre, Le Kremlin Bicêtre, France
[3] Department of Emergency Medicine, Université Pierre et Marie Curie, Groupe Hospitalier Pitié-Salpêtrière, Paris 6, France

* Corresponding author: Département d'Anesthésie-Réanimation, Groupe Hospitalier Nord, Hôpital de la Croix Rousse, 103, Grande-Rue de la Croix Rousse, 69317 Lyon Cedex 04, France. E-mail: frederic.aubrun@chu-lyon.fr

Editor's key points

- Titration of morphine i.v. is used widely for treatment of pain in post-anaesthesia care unit.
- The careful use of a protocol should minimize the adverse effects of morphine.
- Distinguishing between adequate pain relief and morphine-induced sedation can be difficult.
- It can be used with caution in the elderly, children, and obese patients.

Summary. Relief of acute pain during the immediate postoperative period is an important task for anaesthetists. Morphine is widely used to control moderate-to-severe postoperative pain and the use of small i.v. boluses of morphine in the post-anaesthesia care unit allows a rapid titration of the dose needed for adequate pain relief. The essential principle of a titration regimen must be to adapt the morphine dose to the pain level. Although morphine would not appear to be the most appropriate choice for achieving rapid pain relief, this is the sole opioid assessed in many studies of immediate postoperative pain management using titration. More than 90% of the patients have pain relief using a protocol of morphine titration and the mean dose required to obtain pain relief is 12 (7) mg, after a median of four boluses. Sedation is frequent during i.v. morphine titration and should be considered as a morphine-related adverse event and not evidence of pain relief. The incidence of ventilatory depression is very low when the criteria to limit the dose of i.v. morphine are enforced. Morphine titration can be used with caution in elderly patients, in children, or in obese patients. In practice, i.v. morphine titration allows the physician to meet the needs of individual patients rapidly and limits the risk of overdose making this method the first step in postoperative pain management.

Keywords: analgesia, postoperative, analgesic techniques, i.v., analgesics opioid, morphine, pain, acute, titration

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WHY using opioids with caution in obese patients. ?

ESA Mulier 2015

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doi:10.1093/bja/aeq312

BJA

CLINICAL PRACTICE

Dose adjustment of anaesthetics in the morbidly obese

J. Ingrande and H. J. M. Lemmens*

Department of Anesthesia, Stanford University School of Medicine, 300 Pasteur Drive, Room H3576, Stanford, CA 94305, USA

* Corresponding author. E-mail: hlemmens@stanford.edu

Key points

- Morbidly obese patients require special dosing regimens.
- Lean body weight is the optimal scalar for most i.v. opioids and anaesthetics.
- Knowledge of the altered pharmacological behaviour of anaesthetic drugs is essential for optimal management of the morbidly obese.

Anaesthesiologists must be prepared to deal with pharmacokinetic and pharmacodynamic (PD) differences in morbidly obese individuals. As drug administration based on total body weight can result in overdose, weight-based dosing scalars must be considered. Conversely, administration of drugs based on ideal body weight can result in a sub-therapeutic dose. Changes in cardiac output and alterations in body composition affect the distribution of numerous anaesthetic drugs. With the exception of neuromuscular antagonists, lean body weight is the optimal dosing scalar for most drugs used in anaesthesia including opioids and anaesthetic induction agents. The increased incidence of obstructive sleep apnoea and fat deposition in the pharynx and chest wall places the morbidly obese at increased risk for adverse respiratory events secondary to anaesthetic agents, thus altering the PD properties of these drugs. Awareness of the pharmacology of the commonly used anaesthetic agents including induction agents, opioids, inhalation agents and neuromuscular blockers is necessary for safe and effective care of morbidly obese patients.

Keywords: anaesthetics, i.v., pharmacokinetics; anaesthesia, inhalation, pharmacokinetics;

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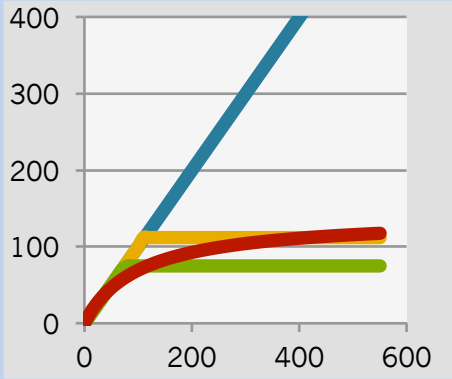
LBW is the optimal scalar for most iv drugs
Knowledge is essential for morbidly obese patients

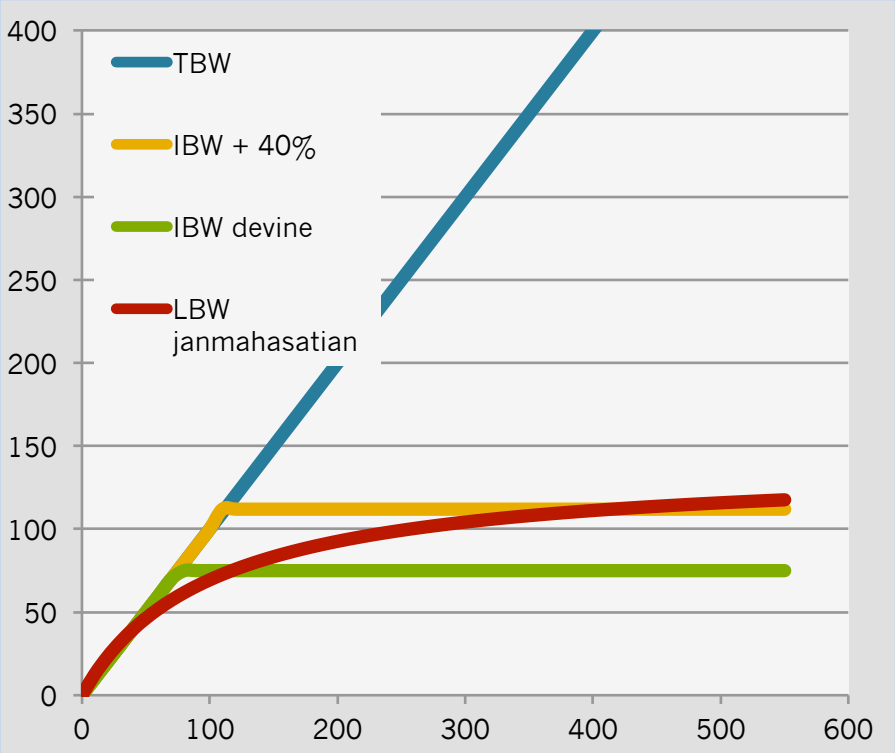
ESA Mulier 2015

Opioids dosing in morbidly obese.



- Fentanyl (dose on LBW)
  - Clearance is higher and increases with LBW
  - Increased CO in obese -> **lower conc during early distribution even when dosed on LBW**
- Sufentanyl (dose above LBW but TBW is too high)
  - Highly lipophilic -> increased distribution volume and elimination half-life, but plasma clearance comparable
    - **Plasma conc are freq lower** than in non obese patients
- Remifentanyl (dose on LBW)
  - Rapidly metabolized, organ dependent clearance.
  - If infusion is based on TBW -> **higher plasma conc** than non obese
  - If infusion is based on LBW -> **faster recovery** than non obese

How does TBW IBW IBW-adj LBW relate for a certain length to TBW?



Kane SP.
Ideal, Adjusted, and Nutritional Body Weight Calculator.
ClinCalc: //clincalc.com/kinetics/idealbw.aspx.
Updated November 20, 2014.

Ideal, Adjusted, and Nutritional Body Weight Calculator - ClinCalc.com

ClinCalc.com

Ideal Body Weight Calculator

Ideal, adjusted, nutritional, BMI, and BSA calculator

Patient Metrics

Height 170 in cm

Body weight 200 kg lbs

Gender Male Female

www.clincalc.com

Reset Calculate

RESULTS

Ideal body weight

65.9 kg

(203% above IBW)

Other Metrics

Adjusted weight	119.5 kg
Nutritional weight	99.4 kg
Lean body weight	85.6 kg
BMI	69.3 kg/m^2
BSA	3.07 m^2

LBW !!!

ESA Muller 2015

A patient's ideal body weight (as described by Devine 1974) may be calculated according to the following equation: [1]

$$Ideal\ BW\ (men) = 50 + 2.3 * (height\ over\ 60\ inches)$$
$$Ideal\ BW\ (women) = 45.5 + 2.3 * (height\ over\ 60\ inches)$$

Kane SP.
Ideal, Adjusted, and Nutritional Body Weight Calculator
ClinCalc: //clincalc.com/kinetics/idealbw.aspx.
Updated November 20, 2014.

Adjusted body weight

This calculator uses an adjustment factor of 0.4, or 40%, to provide an adjusted body weight in patients who are more than 20% of their ideal body weight. This adjustment uses the following equation:

$$AdjustedBW = IdealBW + (0.4 * (ActualBW - IdealBW))$$

Nutritional body weight

This calculator uses an adjustment factor of 0.25, or 25%, to provide a nutritional body weight in patients who are more than 20% of their ideal body weight. Note that some references will use a nutritional body weight on the basis of BMI, rather than percent ideal body weight. [5] This adjustment uses the following equation:

$$NutritionalBW = IdealBW + (0.25 * (ActualBW - IdealBW))$$

Lean body weight

A more accurate measure of lean body weight may be the LBW2005 equation, [6] which unlike the Devine 1974 equation, [1] has been derived and validated from actual patient data. Although this equation is less cited in the literature and less commonly used in practice, it may be a useful alternative in the clinical setting for patients who are particularly short (height < 60 inches) or particularly obese. The LBW2005 uses the following equations:

$$LBW2005\ (men) = \frac{9.27 * 10^3 * ActualBW}{6.68 * 10^3 + (216 * BMI)}$$

$$LBW2005\ (women) = \frac{9.27 * 10^3 * ActualBW}{8.78 * 10^3 + (244 * BMI)}$$

Body mass index (BMI)

BMI is a commonly used measure of obesity outside of the medical setting, but is rarely used within the medical community for clinical decisions. One downfall of the body mass index metric is that it cannot differentiate between lean body weight ("muscle mass") and adipose tissue (fat) because it only takes into account height and weight. The following equation is used to calculate BMI:

$$BMI = \frac{Weight\ in\ kg}{(Height\ in\ meters)^2}$$

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Lippincott Williams & Wilkins

Remifentanil Pharmacokinetics in Obese versus *Lean Patients*

Talmage D. Egan, M.D., Bernou Huizinga, M.D.,† Samir K. Gupta, Ph.D.,‡ Rudy L. Jaarsma, M.D.,†, Richard J. Sperry, M.D., Ph.D.,§ James B. Yee, M.D., Ph.D.,‖ Keith T. Muir, Ph.D.¶*

Background: Remifentanil is a short-acting opioid whose pharmacokinetics have been characterized in detail. However, the impact of obesity on remifentanil pharmacokinetics has not been specifically examined. The goal of this study was to investigate the influence of body weight on remifentanil pharmacokinetics.

Methods: Twelve obese and 12 matched lean subjects undergoing elective surgery received a 1-min remifentanil infusion after induction of anesthesia. Arterial blood samples were collected for determination of remifentanil blood concentrations. Each subject's pharmacokinetic parameters were estimated by fitting a two-compartment model to the concentration *versus* time curves. Nonlinear mixed-effects population models examining the influence of lean body mass (LBM) and total body weight (TBW) were also constructed. Clinical simulations using the final population model were performed.

Results: The obese patient cohort reached substantially higher remifentanil concentrations. The individual pharmacokinetic parameters of a two-compartment model were not significantly different between the obese *versus* lean cohorts (unless normalized to TBW). The final population model scaled central clearance and the central and peripheral distribution volumes to LBM. The simulations illustrated that remifentanil pharmacokinetics are not grossly different in obese *versus* lean subjects and that TBW based dosing in obese patients can result in excessively high remifentanil concentrations.

Conclusions: The essential findings of the study are that remifentanil's pharmacokinetics are not appreciably different in obese *versus* lean subjects and that remifentanil pharmacokinetic parameters are therefore more closely related to LBM than to TBW. Clinically this means that remifentanil dosing regimens should be based on ideal body weight (or LBM) and not TBW. (Key words: Body weight; obesity; opioids; pharmacokinetics; remifentanil.)

Remifentanyl

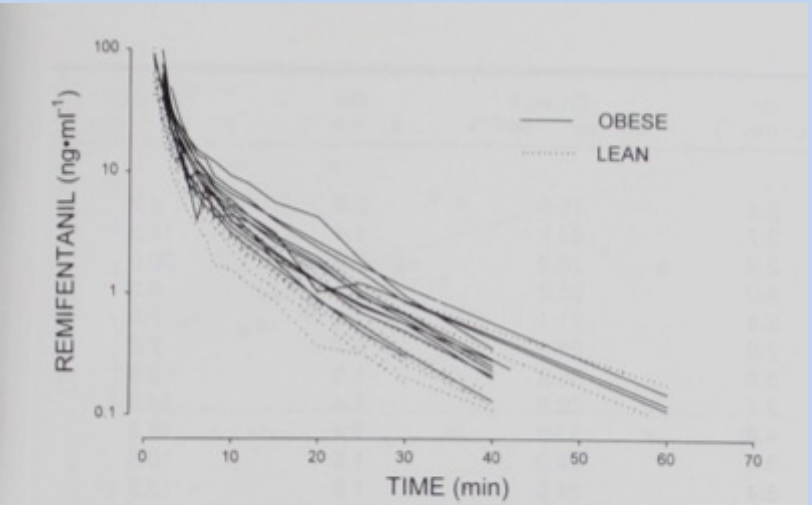

Fig. 1. The raw concentration *versus* time data. The obese subjects' data are plotted with a solid line; lean subjects are represented by the dashed line. Remifentanil concentration is shown on a log scale.

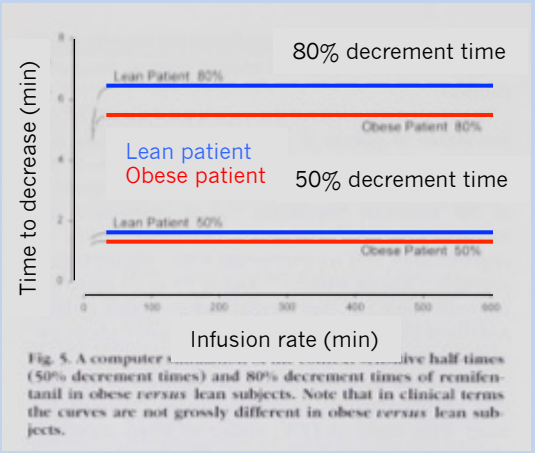

Fig. 5. A computer ... ive half-times (50% decrement times) and 80% decrement times of remifentanil in obese *versus* lean subjects. Note that in clinical terms the curves are not grossly different in obese *versus* lean subjects.

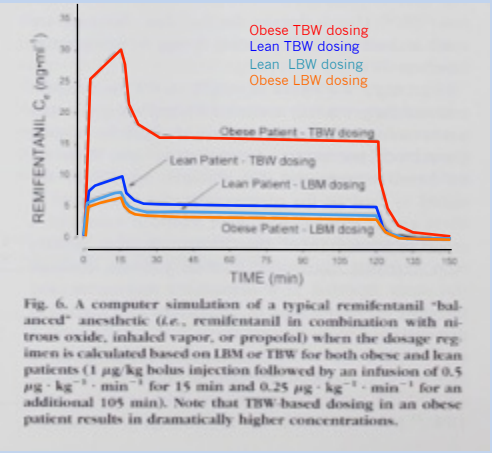

Fig. 6. A computer simulation of a typical remifentanil "balanced" anesthetic (*i.e.*, remifentanil in combination with nitrous oxide, inhaled vapor, or propofol) when the dosage regimen is calculated based on LBM or TBW for both obese and lean patients (1 μg/kg bolus injection followed by an infusion of 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 15 min and 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for an additional 105 min). Note that TBW-based dosing in an obese patient results in dramatically higher concentrations.

Faster recovery in obese patients when dosed on LBW

Opioid dosing peri-operative

	analgesia <	balanced anesthesia <	full sympathicolysis
doses to achieve			
Fentanyl: 10 ug=1mg M+	1 – 2	2 – 20	20 · 50 ug/kg
Sufentanyl:1 ug=1mg M+	0.1 – 0.2	0.2 – 8	8 – 30 ug/kg
Remifentanyl:0.5ug=1mg M+	0.025 – 0.1	0.1 – 0.5	0.5 – 2 ug/kg/min

- Analgesia post operative or anesthesia under spont breathing
- Balanced anesthesia with inhalation or propofol
- Full sympathicolysis with opioid only (stress free)

Adult general anesthesia[1]

Phase	Continuous IV infusion of ULTIVA (mcg/kg/min)	Infusion dose range of ULTIVA (mcg/kg/min)	Supplemental IV bolus dose of ULTIVA (mcg/kg)
Induction (through intubation)	0.5–1[1]		
Maintenance with: Nitrous oxide (66%) Isoflurane (0.4 to 1.5 MAC) Propofol (100 to 200 mcg/kg/min)	 0.4 0.25 0.25	 0.1–2 0.05–2 0.05–2	 1 1 1
Continuation as an analgesic into the immediate postoperative period	0.1	0.025–0.2	Not recommended

[1]An initial dose of 1 mcg/kg may be administered over 30 to 60 seconds.

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ACTA ANAESTHESIOLOGICA SCANDINAVICA
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Intra-operative remifentanil might influence pain levels in the immediate post-operative period after major abdominal surgery

E. G. HANSEN[1,*], T. H. DUEDAHL[2,*], J. RØMSING[2], K.-L. HILSTED[3] and J. B. DAHL[3]
[1]*Department of Anaesthesiology, Herlev University Hospital, Herlev,* [2]*The Danish University of Pharmaceutical Sciences, Copenhagen, and*
[3]*Department of Anaesthesiology, Glostrup University Hospital, Glostrup, Denmark*

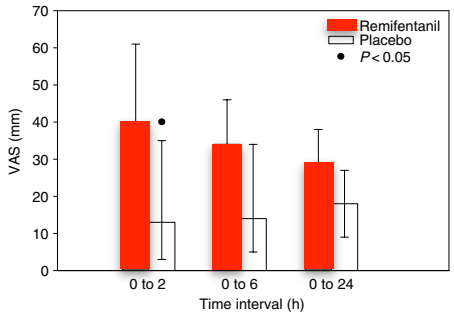


Fig. 2. Visual analogue scale (VAS) scores at rest in the three defined clinically relevant post-operative periods [immediate (0–2 h), early (0–6 h) and late (0–24 h)] after the administration of remifentanil 0.4 μg/kg/min (grey bars) and placebo (white bars) (median, lower and upper quartiles). Within each post-operative period, the observed VAS scores for the specific times were summed and a mean value was calculated for each patient before subsequent statistical evaluation.

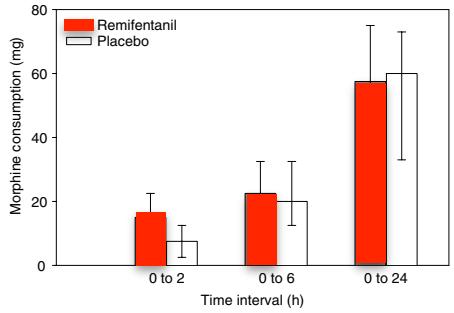


Fig. 4. Morphine consumption in the three defined clinically relevant post-operative periods [immediate (0–2 h), early (0–6 h) and late (0–24 h)] after the administration of remifentanil 0.4 μg/kg/min (grey bars) and placebo (white bars) (median, lower and upper quartiles).

Epi bupivacaine ctu
Epi infusion without PCEA
PCIA only bolus

First hours post op

Placebo had
Lower VAS score
Less extra Morphine with PCIA

Thoracic epidural with bupivacaine 30 mg/h perop -> 10 mg/h postop
Remifentanyl 0.4 ug/kg/min or placebo perop
PCA morphine postop together with thoracic epidural

How to avoid opioids per-operative?

- Stress free anesthesia with full sympathicolysis without opioids
  - Locoregional anesthesia
  - Dexmedetomidine (1 - 2 ug/kg/h)
  - Or lidocaine (3 - 4 mg/kg/h)
  - Magnesium alone not enough (10 - 20 mg/kg/h)

- Balanced anesthesia without opioids
  - multimodal sympathicolysis
    - Dexmedetomidine 0.25 – 0.5 ug/kg idem ug/kg/h
    - + Lidocaine 1.5 mg/kg (or procaine) 1 mg/kg/h
    - + Magnesium 40 mg/kg 5 mg/kg/h
  - + Hypnosis with
    - inhalation 0.8 - 1 MAC
    - Or Propofol 12 mg/kg/h

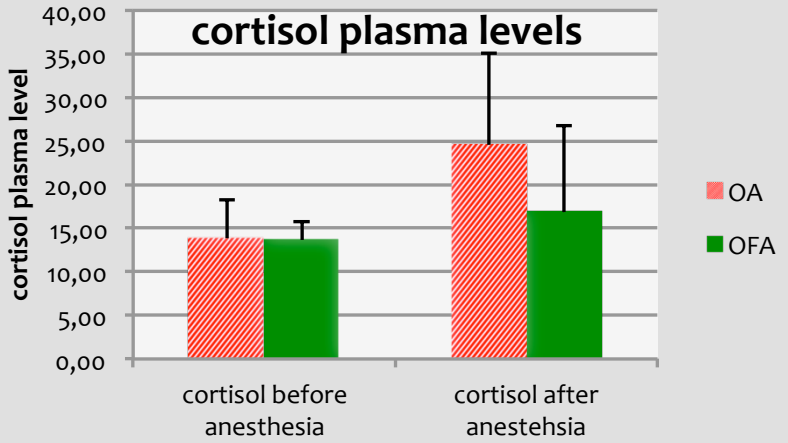
Further opioid reduction by

- Reduce inflammation -> less pain
  - Before surgery starts
    - Steriods: dexamethasone 10 mg or higher dose
    - NSIAD's: diclofenac 150 mg
  - Reduce edema -> less pain
    - Keep patient dry, give fluids only if pulse pressure variation increases.
- Use local wound infiltration with bupivacaine
- ~~Sedatives?~~

Reduce opioid side effects

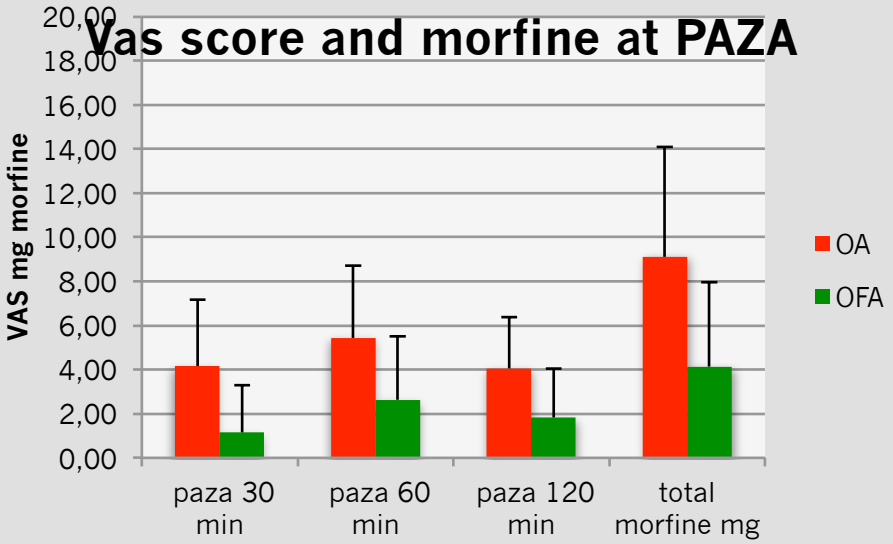
- Reduce tolerance and hyperalgesia
  - Low dose ketamine 10 mg before opioid
  - or 50 mg/10 h
- Reduce PONV
  - Droperidol,
  - Dexamethasone,
  - Ondansetron
  - Empty stomach before extubation

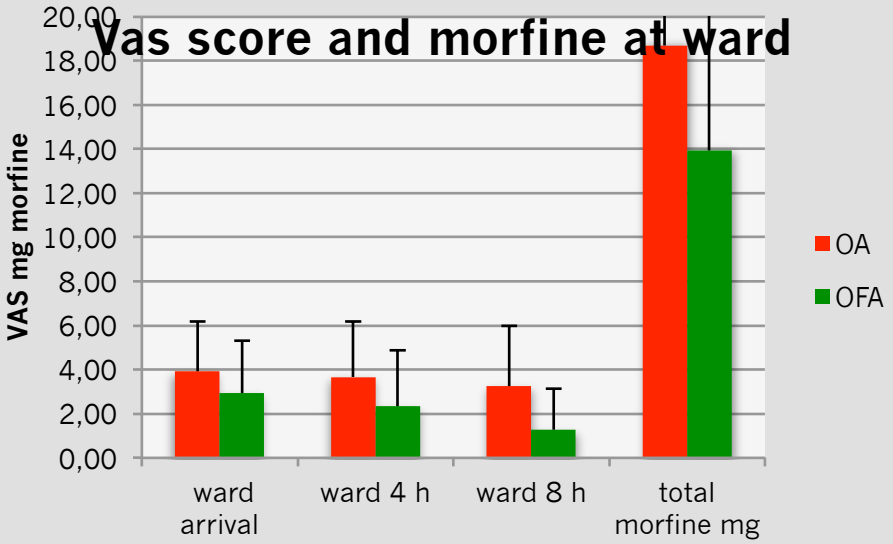
VAS scores are better with a lower morphine consumption post operative



- Randomised study in 40 lap RNY patients
  - Patients got OFA or Opioids per-op only
  - Same post op additive drugs: paracetamol and diclofenac
  - Morphine pump PCIA: VAS score at PAZA and Ward first day

2013 R. Wouters; J. P. Mulier





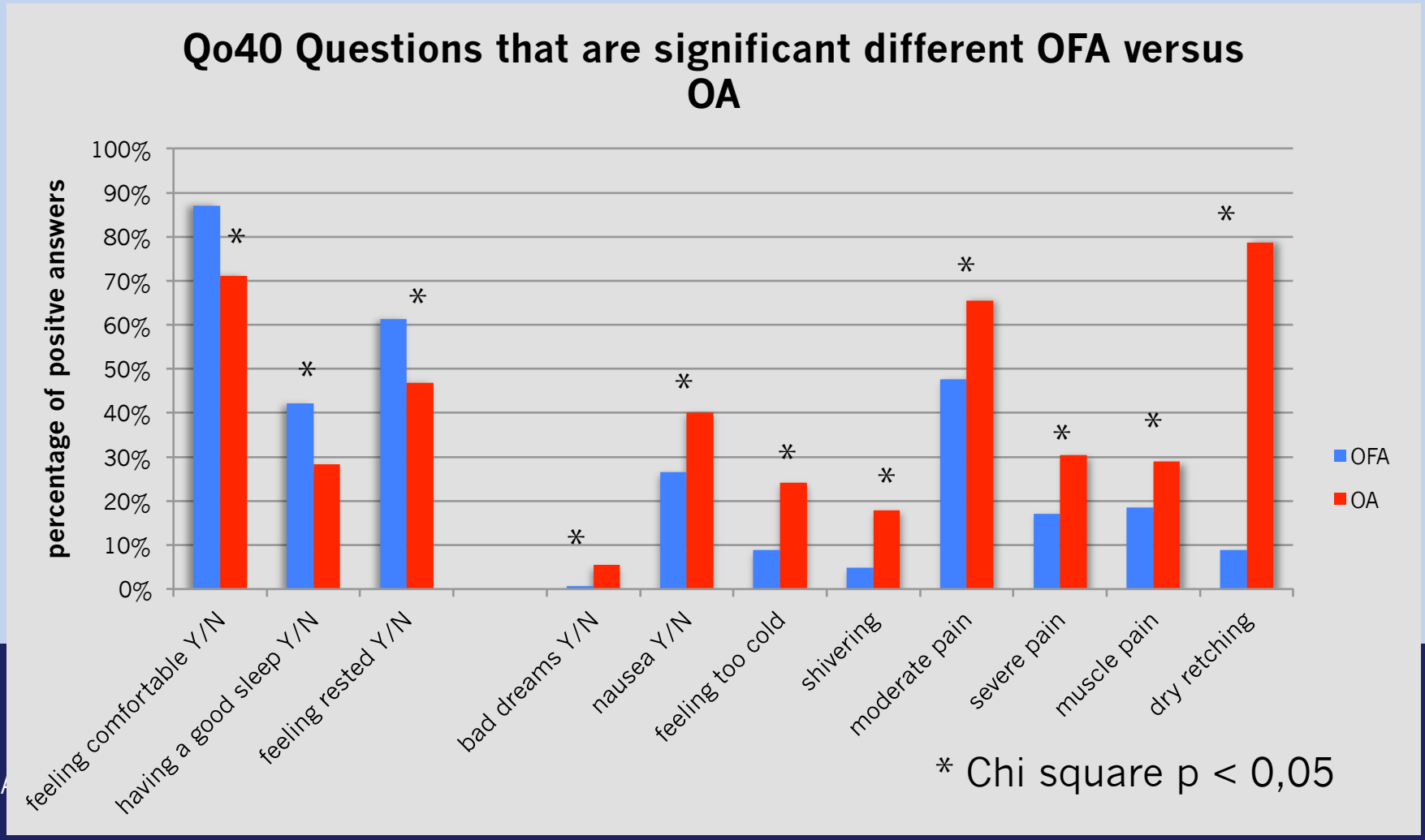
British Journal of Anaesthesia 84 (1): 11–15 (2000)

Validity and reliability of a postoperative quality of recovery score: the QoR-40†

P. S. Myles*, B. Weitkamp, K. Jones, J. Melick and S. Hensen

Department of Anaesthesia and Pain Management, Alfred Hospital, Commercial Road, Prahran, Victoria 3181, Australia

- Observational study in 400 lap RNY patients
  - Patients got OFA or OA per-op and post operative
  - Same post op additive drugs: paracetamol and diclofenac
  - Morphine (or piritramide) as required

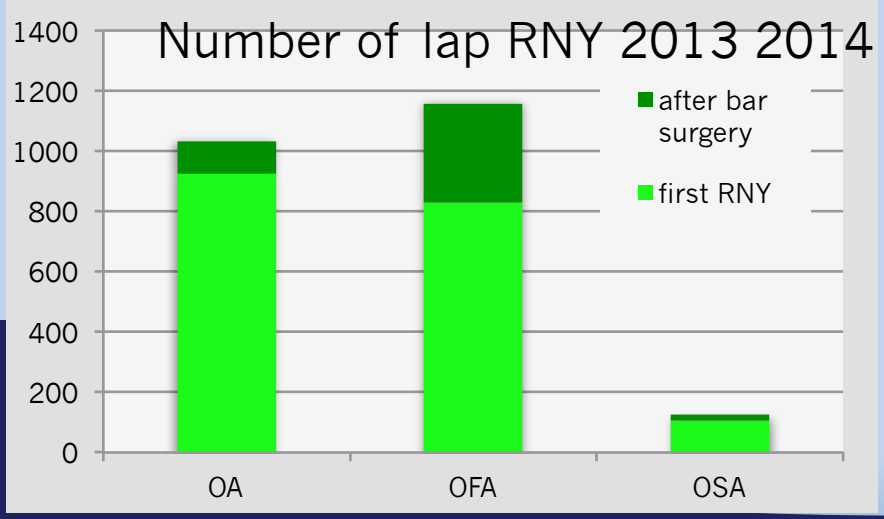


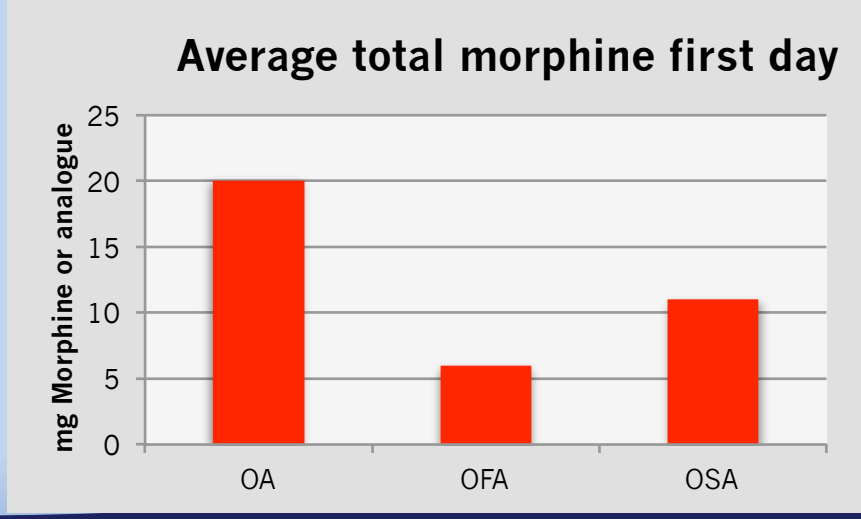
- Observational study in **2318** consecutive lap RNY patients (2012 - 2013)
  - Patients got OFA, OA or OSA per-op and post operative
  - Analgetics according to the perscribing anesthesiologists (NSAIDs, paracetamol and opioids)
  - Total Morphine (or morphine analogue) for day of surgery

10 000 lap RNY in Bruges
on Thursday 30 april 2015
2004 -> 2015

2013 - 2014	OA	OFA	OSA
no complications	994	1124	118
complications	39	35	8
% complications	3,8%	3,0%	6,4%

	OA	OFA	OSA
anesthesia related	3	3	0
bleeding	9	10	2
cardiac	8	**4**	1
infection (non pulm)	3	4	3
Untreatable pain, vomiting	8	**3**	1
respiratory	7	**2**	0
surgical	**1**	8	1
other	0	1	0
total	39	35	8
after bar surgery	7	14	1





Key points to remember

- Lean body weight is the optimal scalar for i.v. Opioids
  - Remifentanyl is easier to dose but faster tolerance
- Loading dose followed by maintenance of short acting
  - Avoid high plasma levels post operative
- Why do you use opioids peri operative?
  - Low dose as analgesia, only effective when awake
  - Medium dose in balanced anesthesia
  - High dose to get full sympathicolysis
- Use an additive to reduce opioids per operative
  - Dexmedetomidine or lidocaine or Magnesium or Ketamine
- Use an aditive to reduce opioids post operative
  - Clonidine and ketamine and Procaine
- Multimodal with all additives to work total opioid free
  - Become ESPCOP member and follow next ESPCOP meeting in Bruges

ESPCOP
The European Society for Perioperative Care of the Obese Patient

www.ESPCOP.org

LIVE OPIOID FREE ANAESTHESIA

December 18th 2015

AZ Sint-Jan AV
Ruddershove 10
Bruges, Belgium

ESA Mulier 2015

ESPCOP
The European Society for Perioperative Care of the Obese Patient

6th ESPCOP meeting

December 19th 2015
Crowne Plaza, Burg 10
Bruges, Belgium

Following the advice in using less peri-operative opioids in morbidly obese patients, it has now become time to discuss "from low-opioid to opioid free" anaesthesia (OFA).

Why, how and when do we use low-opioid or opioid free anaesthesia combined with post-operative multimodal analgesia in morbidly obese patients?

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