

| reference   | participants' characteristics  | intervention group/ control group | outcomes | critical appraisal/ conclusion |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
|---|--|-----------------------------------|----------|--------------------------------|----------|--|--|-------|-------|------|-------------|--|--|------|-------|-----|------------|--|--|------|-------|------|---|----------|----------|---|----------------------|--|--|------|------|------|----------|----------|---|---------|---------|------|---|----------|----------|---|-------------------------|--|--|---------|---------|--------|----------|----------|---|---|---|------|----------|----------|---|--------------------------|--|--|---------|---------|--------|---------------------------|--|--|---------|---------|-------|----------|----------|---|--------------------------|--|--|---|---|------|--|
| <p><a href="#">Nesher et al. 2009</a><br/>Morphine with adjuvant ketamine vs higher dose of morphine alone for immediate postthoracotomy analgesia.<br/>Chest. 2009;136(1):245-252.</p> | <p><b>inclusion criteria</b></p> <ul style="list-style-type: none"> <li>- first-time isolated coronary bypass</li> <li>- if patient's surgeon considered them candidates for a MIDCAB procedure, - if patient were to undergo lung surgery</li> </ul> <p><b>exclusion criteria</b></p> <ul style="list-style-type: none"> <li>- ASA physical status ≥III</li> <li>- undergone emergency surgery</li> <li>- Q-wave myocardial infarct occurring during the previous 3 weeks</li> <li>- poor left ventricular function</li> <li>- BMI &gt;35 kg/m<sup>2</sup></li> <li>- past or current neuropathy</li> <li>- psychological disturbances</li> <li>- use of psychiatric medications, including antidepressants and antipsychotic agents</li> <li>- chronic liver or renal failure requiring dialysis</li> <li>- FEV<sub>1</sub>/FVC &lt;70%</li> <li>- allergy to ketamine, morphine, or NSAIDs</li> <li>- clotting abnormalities</li> <li>- platelet count &lt;70,000/μL</li> <li>- WBC count &lt;3,000 μL or &gt;14,000/μL</li> <li>- uncontrolled diabetes mellitus or fasting blood glucose&gt;250 g/dL</li> <li>- evidence of sepsis or infection up to 1 week prior to randomisation</li> </ul> <p><b>demographic data:</b></p> <table border="1"> <thead> <tr> <th>group MO</th> <th>group MK</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>age, yr*</td> <td></td> <td></td> </tr> <tr> <td>58±12</td> <td>61±11</td> <td>0.41</td> </tr> <tr> <td>weight, kg*</td> <td></td> <td></td> </tr> <tr> <td>73±8</td> <td>76±14</td> <td>0.4</td> </tr> <tr> <td>sex (m/f)*</td> <td></td> <td></td> </tr> <tr> <td>13/9</td> <td>10/12</td> <td>0.16</td> </tr> </tbody> </table> <p>*Including data of the excluded patients (MO: n=2; MK: n= 1)</p> <p><b>patient flow and follow up:</b></p> <p><u>total patient number included:</u><br/>44</p> <p><u>randomised in:</u><br/>group MO: 22<br/>group MK: 22</p> <p><u>excluded:</u><br/>group MO: 2<br/>group MK: 1</p> <p><u>analysed:</u><br/>group MO: 20<br/>group MK: 21</p> <p><u>follow-up:</u><br/>0, 15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, 180, 195, 210, 225, 240 mins</p> | group MO                          | group MK | p                              | age, yr* |  |  | 58±12 | 61±11 | 0.41 | weight, kg* |  |  | 73±8 | 76±14 | 0.4 | sex (m/f)* |  |  | 13/9 | 10/12 | 0.16 | <p><b>intervention prior to anaesthesia</b></p> <ul style="list-style-type: none"> <li>- not reported</li> </ul> <p><b>mode of anaesthesia</b></p> <ul style="list-style-type: none"> <li>- fentanyl</li> </ul> <p><b>surgical approach</b></p> <ul style="list-style-type: none"> <li>- thoracotomy for minimally invasive direct coronary artery bypass or for lung tumor resection</li> </ul> <table border="1"> <thead> <tr> <th>group MO</th> <th>group MK</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>MIDCAB/lung surgery*</td> <td></td> <td></td> </tr> <tr> <td>7/15</td> <td>6/16</td> <td>0.25</td> </tr> </tbody> </table> <p>Duration of surgery, h*</p> <table border="1"> <thead> <tr> <th>group MO</th> <th>group MK</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>3.1±1.3</td> <td>3.5±1.0</td> <td>0.28</td> </tr> </tbody> </table> <p><b>supplemental analgesia</b></p> <ul style="list-style-type: none"> <li>- 75 mg IM diclofenac, as rescue</li> </ul> <p><b>postoperative analgesia</b></p> <ul style="list-style-type: none"> <li>- group MO (morphine only): IV PCA delivering 1.5 mg morphine plus saline solution</li> <li>- group MK (morphine + ketamine): IV PCA delivering 1.0 mg of morphine plus a 5 mg ketamine bolus, with a 7 min lo</li> </ul> | group MO | group MK | p | MIDCAB/lung surgery* |  |  | 7/15 | 6/16 | 0.25 | group MO | group MK | p | 3.1±1.3 | 3.5±1.0 | 0.28 | <p><b>postoperative pain [VAS]: mean (±SD)</b></p> <table border="1"> <thead> <tr> <th>group MO</th> <th>group MK</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>Maximal pain (VAS 0–10)</td> <td></td> <td></td> </tr> <tr> <td>5.6±1.0</td> <td>3.7±0.7</td> <td>0.0001</td> </tr> </tbody> </table> <p><b>diclofenac consumption (n)</b></p> <table border="1"> <thead> <tr> <th>group MO</th> <th>group MK</th> <th>p</th> </tr> </thead> <tbody> <tr> <td>4</td> <td>1</td> <td>0.14</td> </tr> </tbody> </table> <p><b>consumption of morphine [mg]: mean±SD</b></p> <table border="1"> <thead> <tr> <th>group MO</th> <th>group MK</th> <th>p</th> </tr> </thead> <tbody> <tr> <td><u>first-hour postop</u></td> <td></td> <td></td> </tr> <tr> <td>6.8±1.9</td> <td>3.7±1.2</td> <td>0.0001</td> </tr> <tr> <td><u>second-hour postop</u></td> <td></td> <td></td> </tr> <tr> <td>5.5±3.6</td> <td>2.8±2.3</td> <td>0.008</td> </tr> </tbody> </table> <p><b>adverse effects/ events (n)</b></p> <table border="1"> <thead> <tr> <th>group MO</th> <th>group MK</th> <th>p</th> </tr> </thead> <tbody> <tr> <td><u>incidence of PONV</u></td> <td></td> <td></td> </tr> <tr> <td>3</td> <td>1</td> <td>0.24</td> </tr> </tbody> </table> | group MO | group MK | p | Maximal pain (VAS 0–10) |  |  | 5.6±1.0 | 3.7±0.7 | 0.0001 | group MO | group MK | p | 4 | 1 | 0.14 | group MO | group MK | p | <u>first-hour postop</u> |  |  | 6.8±1.9 | 3.7±1.2 | 0.0001 | <u>second-hour postop</u> |  |  | 5.5±3.6 | 2.8±2.3 | 0.008 | group MO | group MK | p | <u>incidence of PONV</u> |  |  | 3 | 1 | 0.24 | <p><b>methodological shortcomings</b></p> <ul style="list-style-type: none"> <li>- method used to implement the random allocation sequence not reported</li> <li>- not reported whether the sequence was adequately concealed until interventions were assigned</li> <li>- method used to generate the random allocation sequence not reported</li> <li>- not reported how the sequence was concealed until interventions were assigned</li> </ul> <p><b>level of evidence: 1</b></p> <p><b>authors' conclusion</b></p> <p>"immediate (4 h) postoperative subanaesthetic doses of ketamine added to two thirds the standard dose of morphine provided equivalent analgesia with a better safety profile compared to that obtained by a standard dose of morphine alone in patients undergoing thoracotomy"</p> |
| group MO  | group MK   | p                                 |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| age, yr*  |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 58±12   | 61±11  | 0.41                              |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| weight, kg*   |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 73±8  | 76±14  | 0.4                               |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| sex (m/f)*  |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 13/9  | 10/12  | 0.16                              |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| group MO  | group MK   | p                                 |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| MIDCAB/lung surgery*  |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 7/15  | 6/16   | 0.25                              |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| group MO  | group MK   | p                                 |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 3.1±1.3   | 3.5±1.0  | 0.28                              |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| group MO  | group MK   | p                                 |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| Maximal pain (VAS 0–10)   |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 5.6±1.0   | 3.7±0.7  | 0.0001                            |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| group MO  | group MK   | p                                 |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 4   | 1  | 0.14                              |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| group MO  | group MK   | p                                 |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| <u>first-hour postop</u>  |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 6.8±1.9   | 3.7±1.2  | 0.0001                            |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| <u>second-hour postop</u>   |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 5.5±3.6   | 2.8±2.3  | 0.008                             |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| group MO  | group MK   | p                                 |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| <u>incidence of PONV</u>  |  |                                   |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |
| 3   | 1  | 0.24                              |          |                                |          |  |  |       |       |      |             |  |  |      |       |     |            |  |  |      |       |      |   |          |          |   |                      |  |  |      |      |      |          |          |   |         |         |      |   |          |          |   |                         |  |  |         |         |        |          |          |   |   |   |      |          |          |   |                          |  |  |         |         |        |                           |  |  |         |         |       |          |          |   |                          |  |  |   |   |      |  |