**Supplementary Digital Content**

**Figure S1.** Forest plot of 6-months mortality in levosimendan vs. dobutamine group. The center of each square represents the weighted odds ratio for individual trials, and the corresponding horizontal line stands for 95% confidence interval. The diamonds represent pooled results. Procedure time presented in seconds.



**Figure S2.** Forest plot of length of stay in hospital in levosimendan vs. dobutamine group. The center of each square represents the weighted mean difference for individual trials, and the corresponding horizontal line stands for 95% confidence interval. The diamonds represent pooled results. Procedure time presented in seconds.



**Table S1.** Characteristics of included studies

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Country** | **Study design** | **Treatment** | **No. of patients** | **Age** | **Sex, male** | **BMI (kg/m2)** | **LVEF (%)** | **NYHA class IV** |
| Bergh et al. 2010 | Sweden | multinational, randomized, double-blind, phase IV study | Levosimendan | 29 | 70 ± 10 | 26 | 27.0 ± 5.4 | 21.2 ± 5.8 | 12 |
| Dobutamine | 31 | 71 ± 11 | 25 | 25.7 ± 4.0 | 21.8 ± 6.1 | 15 |
| Bonios et al. 2012 | Greece | randomized, open-labeled study | Levosimendan | 21 | 55 ± 12 | 20 | NS | 23 ± 7 | NS |
| Dobutamine | 21 | 53 ± 13 | 20 | NS | 21 ± 5 | NS |
| Duygu et al 2008 (a) | Turkey | Randomized study | Levosimendan | 20 | 62 ± 10 | 11 | NS | 28 ± 5 | 12 |
| Dobutamine | 20 | 64 ± 8 | 10 | NS | 30 ± 6 | 11 |
| Duygu et al. 2008 (b) | Turkey | Randomized study | Levosimendan | 30 | 64 ± 10 | 19 | NS | 27 ±7 | 12 |
| Dobutamine | 30 | 65 ± 8 | 16 | NS | 25 ± 7 | 9 |
| Fedele et al. 2011 | Italy | Observational study | Levosimendan | 147 | 66.06 ± 13 | 115 | NS | NS | NS |
| Dobutamine | 145 | 68.06 ± 11.06 | 114 | NS | NS | NS |
| Follath et al. 2002 | Multi-country | Multicentre, randomised, double-blind, doubledummy, parallel-group trial | Levosimendan | 103 | 58 ± 11 | 91 | NS | NS | NS |
| Dobutamine | 100 | 60 ± 11 | 85 | NS | NS | NS |
| Madeira et al. 2017 | Portugal | Retrospective study | Levosimendan | 77 | 64 ± 14 | 62 | NS | 27 ± 9 | NS |
| Dobutamine | 31 | 73 ± 16 | 18 | NS | 35 ± 12 | NS |
| Mebazza et al. 2007 | Multi-country | Randomized, double-blind trial | Levosimendan | 664 | 67 ± 12 | 493 | NS | 24 ± 5 | 572 |
| Dobutamine | 663 | 66 ± 12 | 463 | NS | 24 ± 5 | 562 |
| Nieminen et al. 2000 | Multi-country | A double-blind, placebo-controlled, randomized, multicenter, parallel-group study | Levosimendan | 95 | 63 ± 2.5 | 82 | NS | 26 ± 2 | 3 |
| Dobutamine | 20 | 63 ± 2 | 19 | NS | 24 ± 2 | 1 |
| Yontar et al. 2010 | Turkey | Randomized study | Levosimendan | 36 | 66.1 ± 10.5 | NS | 23.15 ± 8.3 | NS | NS |
| Dobutamine | 22 | 67 ± 6.9 | NS | 24.56 ± 7.5 | NS | NS |

Legend: BMI = Body Mass Index; NYHA = New York Heart Association functional class; LVEF = Left ventricular ejection fraction; NS = Not specified.

**Table S2**. Characteristics of adverse events in levosimendan vs. dobutamine group.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** | **No. of studies** | **Events in Levosimendan group** | **Events in Dobutamine group** | **OR (95%CI)** | **P value** | **I2 statistic** |
| Any adverse event | 3 | 588/792(74.2%) | 565/791(71.4%) | 1.17 (0.93, 1.47) | 0.18 | 0% |
| Any serious adverse event | 2 | 196/763(25.7%) | 222/760(29.2%) | 0.83 (0.66, 1.05) | 0.13 | 47% |
| Hypotension | 3 | 121/792(15.3%) | 98/791(12.4%) | 2.14 (0.76, 5.99) | 0.15 | 68% |
| Cardiac arrest | 2 | 21/763(2.8%) | 27/760(3.6%) | 0.77 (0.43, 1.38) | 0.38 | 0% |
| Cardiac failure | 2 | 84/689(12.2%) | 116/691(16.8%) | 0.69 (0.51, 0.93) | **0.02** | 0% |
| Congestive cardiac failure | 1 | 26/660(3.9%) | 22/660(3.3%) | 1.19 (0.67, 2.12) | 0.78 | NA |
| Cardiogenic shock | 1 | 15/660(2.3%) | 23/660(3.5%) | 0.64 (0.33, 1.25) | 0.19 | NA |
| Hypokalemia | 1 | 15/660(2.3%) | 16/660(2.4%) | 0.94 (0.46, 1.91) | 0.86 | NA |
| Atrial fibrillation | 2 | 62/763(8.1%) | 41/760(5.4%) | 1.56 (1.04, 2.35) | **0.03** | 0% |
| Ventricular tachycardia | 2 | 53/763(6.9%) | 50/760(6.6%) | 1.06 (0.71, 1.59) | 0.76 | 0% |
| Ventricular extrasystoles | 2 | 41/763(5.4%) | 27/760(3.6%) | 1.55 (0.94, 2.54) | 0.09 | 50% |
| Tachycardia | 1 | 33/660(5.0%) | 33/660(5.0%) | 1.00 (0.61, 1.64) | 1.0 | NA |
| Angina pectoris | 1 | 12/660(1.8%) | 13/660(2.0%) | 0.92 (0.42, 2.04) | 0.84 | NA |
| Bradycardia | 2 | 9/763(1.2%) | 18/760(2.4%) | 0.49 (0.22, 1.10) | 0.09 | 0% |
| SVT | 1 | 0/103(0.0%) | 3/100(3.0%) | 0.13 (0.01, 2.64) | 0.19 | NA |
| Chest pain | 1 | 32/660(4.8%) | 47/660(7.1%) | 0.66 (0.42, 1.06) | 0.08 | NA |
| Headache | 2 | 69/763(9.0%) | 36/760(4.7%) | 2.00 (1.32, 3.03) | **0.001** | 0% |
| Nausea | 2 | 49/689(7.1%) | 49/691(7.1%) | 1.00 (0.67, 1.51) | 0.99 | 63% |
| Insomnia | 2 | 41/689(6.0%) | 32/681(4.7%) | 1.26 (0.78, 2.03) | 0.34 | 0% |
| Diarrhea | 1 | 30/660(4.5%) | 21/660(3.2%) | 1.45 (0.82, 2.56) | 0.20 | NA |
| Vomiting | 1 | 22/660(3.3%) | 24/660(3.6%) | 0.91 (0.51, 1.65) | 0.76 | NA |
| Pulmonary edema | 1 | 20/660(3.0%) | 18/660(2.7%) | 1.11 (0.58, 2.13) | 0.74 | NA |
| Pneumonia | 1 | 30/660(4.5%) | 24/660(3.6%) | 1.26 (0.73, 2.18) | 0.41 | NA |
| Renal failure | 1 | 24/660(3.6%) | 22/660(3.3%) | 1.09 (0.61, 1.97) | 0.76 | NA |
| Urinary tract infection | 2 | 24/689(3.5%) | 31/691(4.5%) | 0.77 (0.45, 1.33) | 0.35 | 43% |
| Dizziness | 2 | 19/763(2.5%) | 17/760(2.2%) | 1.12 (0.58, 2.14) | 0.74 | 0% |
| Anemia | 1 | 15/660(2.3%) | 17/660(2.2%) | 0.88 (0.44, 1.78) | 0.72 | NA |
| Hyperkalemia | 1 | 15/660(2.3%) | 16/660(2.4%) | 0.94 (0.46, 1.91) | 0.86 | NA |

**Full list of publications included in the meta-analysis:**

1. Bergh CH, Andersson B, Dahlstrom U, et al. Intravenous levosimendan vs. dobutamine in acute decompensated heart failure patients on beta-blockers. European Journal of Heart Failure 2010; 12:404–410. doi:10.1093/eurjhf/hfq032.
2. Bonios MJ, Terrovitis JV, Drakos SG, et al. Comparison of three different regimens of intermittent inotrope infusions for end stage heart failure. Int J Cardiol. 2012; 159(3):225-9. doi: 10.1016/j.ijcard.2011.03.013.
3. Duygu H, Turk U, Ozdogan O, et al. Levosimendan versus Dobutamine in Heart Failure Patients Treated Chronically with Carvedilol. Cardiovasc Ther. Fall 2008; 26(3):182-8. doi: 10.1111/j.1755-5922.2008.00050.x.
4. Duygu H, Nalbantgil S, Ozerkan F, et al. Effects of Levosimendan on Left Atrial Functions in Patients with Ischemic Heart Failure. Clin Cardiol. 2008; 31(12):607-13. doi: 10.1002/clc.20332.
5. Fedele F, D’Ambrosi A, Bruno N, et al. Cost-effectivenessofLevosimendaninPatientsWithAcute Heart Failure. J Cardiovasc Pharmacol 2011; 58(4): 363-366.
6. Follath F, Cleland JGF, Just H, et al. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial. Lancet. 2002; 360(9328):196-202. doi: 10.1016/s0140-6736(02)09455-2.
7. Madeira M, Caetano F, Almeida I, et al. Inotropes and cardiorenal syndrome in acute heart failure - A retrospective comparative analysis. Rev Port Cardiol. 2017; 36(9):619-625. doi: 10.1016/j.repc.2017.03.006.
8. Mebazaa A, Nieminen MS, Packer M, et al. Levosimendan vs dobutamine for patients with acute decompensated heart failure: the SURVIVE Randomized Trial. JAMA. 2007 May 2;297(17):1883-91. doi: 10.1001/jama.297.17.1883.
9. Nieminen MS, Akkila J, Hasenfuss G, et al. Hemodynamic and Neurohumoral Effects of Continuous Infusion of Levosimendan in Patients With Congestive Heart Failure. J Am Coll Cardiol. 2000; 36(6):1903-12. doi: 10.1016/s0735-1097(00)00961-x.
10. Yontar OC, Yilmaz MB, Yalta K, Erdem A, Tandogan I. Acute effects of levosimendan and dobutamine on QRS duration in patients with heart failure. Arq Bras Cardiol. 2010; 95(6):738-42. doi: 10.1590/s0066-782x2010005000143.