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|  **eTable 1. Overview of studies assessing the association between lactate and various outcomesa,b** |
| **Study** | **Sites** | **Period** | **Designc** | **Inclusion criteria** | **Exclusion criteria** | **Sample size** | **Lactated** | **Outcome(s)** | **Results** |
| **Where** | **When** | **High?** |
| Schütz 1998 1 | 1 | Oct. 1992 – Dec. 1996 | NR | Open heart surgery | - | 4,640 | Serum | NR | NR | Mesenteric ischemia | 0.3% developedmesenteric ischemia all with elevated lactate. Lactate not reported in those without mesenteric ischemia |
| Demers 2000 2 | 1 | Jan. – Dec. 1995 | Retrospective | Cardiac surgery with CPB | Intraoperative death, pre-operative lactate > 2.5, missing data | 1,259 | Arterial | Highest during surgery | > 4.0 | Hospital mortality, post-operative complications, LOS | 18% with high lactate. 11.0% versus 1.4% mortality, more complications, longer LOS |
| Davies 2001 3 | 1 | 2-year period | Retrospective | Cardiac surgical patients with IABP | - | 39 | Serum | Within 8 hours of IABP support | > 10 | Survival to discharge, inability to wean from IABP | Associated with both outcomes. 100% PPV and 53% NPV for mortality |
| Rao2001 4 | 1 | 1983 - 1996 | Prospective | CABG | - | 623 | Difference between arterial and coronary sinus | During surgery | 0.4(lactate release) | Low cardiac output syndrome (IABP or inotropes) | Myocardial lactate release higher in those with the outcome and in those that died. AUC: 0.63.  |
| Byhahn 2001 5 | 1 | 1-year period | Prospective | Cardiac surgery with CPB | - | 1,116 | NR | NR | NR | Gastro-intestinal complications  | 2.1% developed the outcome. Patients with necrotic bowel or hepatic failure had elevated lactate (70% > 10), others normal  |
| Klotz 2001 6 | 1 | Nov. 1997 – Jul. 1999 | NR | Cardiac surgery with CPB | - | 20 | Serum | NR | NR | Non-occlusivemesenteric ischemia | The 20 represented 0.6% of all. Non-significant relationship between severity and lactate  |
| Takami 2002 7 | 1 | NR | NR | Cardiac surgery | - | 65 | Trans-pulmonary arterio-venousdifference | Arrival to ICU | NR | Not clearly defined | Associated with duration of intubation and post-op oxygenation |
| Dixon 2003 8 | 1 | NR | Prospective | Elective CABG with CPB | Multiple including high creatinine, bilirubin, temperature or white cell count, airway disease  | 40 | Arterial | 4, 7, 10, 13, and 16 hours after CPB | NR | Hours of ventilation, ICU LOS | Not associated with the outcomes |
| Maillet 2003 9 | 1 | 6-month period  | Prospective | Cardiac surgery with normo-thermic CPB | Off-pump ssurgery | 325 | Arterial | 4 measurements within the first day of ICU | > 3.0 defined as early and late | ICU mortality, LOS and complications | 21% had early high lactate, 17% had late. Both associated with all outcomes. AUC for ICU mortality for early: 0.85 (69% sens., 81% spec. for predefined cut-off). AUC for late: 0.72 (62% sens., 75% spec. for predefined cut-off) |
| Toraman2004 10 | 1 | Feb. 1999 – Feb. 2002 | Prospective | CABG | Hepatic dysfunction | 776 | Serum | Within half an hour after surgery | > 2.0 | IABP, inotropes, time to extubation, LOS, mortality | 31% had high lactate. Associated with all outcomes  |
| Huwer 2004 11 | 1 | Jan. 1999 - 2002 | Retrospective | Cardiac surgery with CPB | - | 3,600 | Serum | NR | NR | Mesenteric ischemia | 0.6% with mesenteric ischemia. Lactate higher in those with the outcome. |
| Shinde 2005 12 | 1 | NR | Prospective | Valve heart surgery with CPB | Diabetic patients onphenformin | 82 | Arterial  | During and after | Change in lactate > 4 | Duration of inotropic support and mechanical ventilation | High lactate associated with the outcomes |
| Heringlake 2005 13 | 1 | NR | Prospective | CABG | - | 20 | Myocardial | During | NR | Hemodynamics | Some weak and some significant associated with hemodynamic parameters.  |
| Hekmat2005 14 | 1 | Apr. 1999 – Feb. 2003 | Prospective | Cardiac surgery | < 24 hours ICU stay | 2545 | Blood | NR | Various | Mortality | Included in prediction score with good calibration and discrimination |
| Zhang 2006 15  | 1 | Jan. 1996 – Oct. 2004 | NR | ECMO for post-cardiotomy cardiogenicshock  | - | 32 | NR | 48 hours after ECMO | NR | Weaning off ECMO | Higher lactates in the non-weaning group |
| Svenmarker2006 16 | 1 | 2000 - 2005 | Retrospective | Cardiac surgery with CPB | - | 5,121 | Arterial | Termination of CPB | > 90th percentile (2.0) | Mortality, LOS, complication | Increase in all outcomes in those with high lactate. Sens.: 54%, spec.: 98% for the cut-off  |
| Ranucci 2006 17 | 1 | Sept. 2005 –Dec. 2005 | Prospective | Cardiac surgery with CPB | Pre-operative lactate > 2.0 | 470 | Arterial  | During CPB | > 3.0 | LOS, complication, mortality | 5.7% had high lactate. Associated with ICU LOS, prolonged mechanical ventilation, IAPB, morbidity. Not associated with mortality in multivariable analysis |
| Oshima2007 18 | 1 | Jan. 1991 – Sept. 2008 | Retrospective | Percutaneous cardio-pulmonary support system after cardiac surgery with CPB | - | 13 | Serum | Start of support and 12, 24, 48, 72, and 96 hours after | NR | Weaning from percutaneous support | Only significant difference at 96 hours |
| Abarbanell2008 19 | 1 | Jan. 1998 – Dec. 2004 | Retrospective | Cardiac surgery for congenital disease (adults)  | - | 234 | Blood | Initial and 24 hours | NR | Mortality, LOS, complications | Lactate associated with mortality only in univariate analysis |
| Hauer 2009 20 | 1 | Jan. 2003 – Dec. 2005 | Prospective | Cardiac surgery with CPB | Heart transplant, minimally invasive procedures, preoperative chronic renaldysfunction | 1,531 | Serum | Hourly, highest within 12 hours | > 1.1 | RRT | 4.6% had the outcome. Higher max. lactate in those with the outcome. Sens.: 49%, Spec.: 99%. Non-survivors on RRT had higher max. lactate |
| Boeken 2009 21 | 1 | Jan. 2004 – Jan. 2008 | Retrospective | IABP after cardiac surgery with CPB | - | 223 | Serum  | Max. first 10 hours | > 11 | Mortality, post-operative complications | Associated with the outcomes  |
| Gasparovic2010 22 | 1 | May 2007 – May 2008 | Prospective | CABG with CPB | Valve surgery, redo surgery, prior history of AF | 215 | Radial artery – venous coronary | During CPB | NR | AF | 26% had the outcome. No difference between groups |
| Nogueira2010 23 | 1 | Jan. 2004 – Aug. 2005 | Prospective | Cardiac surgery with CPB | Missing data, pre-operative sepsis, or death within 3 days | 246 | Arterial or venous | Arrival to ICU, 6 hours and 24 hours | NR | Organ dysfunction of the 3rd post-operative day  | Lactate at 24 hours associated with the outcome in multivariable analysis, others not.  |
| Rastan 2010 24 | 1 | May 1996 - 2008 | Prospective | ECMO after cardiac surgery | - | 517 | NR | End of surgery, start of ECMO, 24 and 48 hours after | > 4/10 | Mortality | Lactate at all time points associated with outcomes |
| Ranucci 2010 25 | 1 | 2009 | Retrospective | Cardiac surgery with CPB | Missing data, congenital heart disease  | 929 | Arterial  | ICU admission | > 4 | Mortality | Higher in non-survivors. Remained in multivariable models. For cut-off 4: Sens.: 22%, spec. 98%, PPV: 22%, NPV: 98%. Marginally improved previous prediction scores |
| Kapoor 2011 26 | 1 | NR | Prospective | Elective CABG or valve surgery with CPB | Multiple including pre-operative conditions and concomitant valve and CABG surgery | 40 | Coronary sinus and plasma | Before, during, and after CPB | > 2.9 (myo-cardial lactate) | LOS and inotrope requirements | Longer ICU stay, baseline lactate associated with use of inotropes |
| Noval-Padillo2011 27 | 1 | Jan. – Dec. 2010  | Prospective | Heart transplant | - | 16 | Arterial | Before, during, and after CPB (ICU arrival) | > 4 | Complication and mortality | 56% had high lactate at ICU arrival. Associated with complications |
| Čanádyová2012 28 | 1 | May 2000 – May 2006 | Retrospective | Cardiac surgery with re-exploration for bleeding or tamponade | - | 152 | NR | NR | NR | Death | Lactate higher in non-survivors |
| Hu2012 29 | 1 | Oct. 2007 – Jun. 2008 | Prospective | CABG or valve surgery with CPB with central venous catheter | Multiple including off-pump surgery and intra-operative complications | 60 | Blood | Arrival to ICU and 24 hours later | > 4 | LOS, organ failure | Lactate at 24 hours associated with outcomes, not at ICU arrival. Remained in multivariable analysis |
| Kogan2012 30 | 1 | Aug. 2009 – Jul. 2011 | Prospective | Cardiac surgery | Off-pump surgery, liver disease | 1,820 | Arterial | Arrival to ICU, every 1-3 hours for 24 hours. Peak value | Mode-rate: 2.2–4.4High: > 4.4 | LOS, complications, mortality | Normal: 18%, Moderate: 58%High: 24% Associated with some complication, ICU LOS, mortality but not hospital LOS (almost significant) |
| Nicolini2013 31 | 1 | Feb. 2009 – Aug. 2010 | Prospective | Cardiac surgery | Multiple including off-pump surgery, missing data and pre-operative neurological dysfunction | 954 | Blood | End-CPB and peak in ICU | NR | Cerebral complications | 9.9% had the outcome. Peak in the ICU was higher in those with the outcome. End-CPB lactate was associated with the outcome in multivariable analysis |
| Slottosch2013 32 | 1 | Jan. 2006 – Dec. 2010 | Retrospective | ECMO after cardiac surgery for shock | Central thoracic ECMO, ECMO for other reasons | 77 | NR | 24 hours after ECMO | NR | Death | Higher in non-survivors. Remained in multivariable analysis |
| Lindsay2013 33 | 1 | Jan. 2008 – Aug. 2008 | Retrospective | CABG, valve surgery, or combined | < 2 lactate measurements within 12 hours after surgery | 1,291 | Arterial. Predicted lactate clearance time | First 12 hours post-operatively | NR | LOS, complications, mortality | Associated with the outcomes. Remained in multivariable analysis  |
| Groesdonk2013 34 | 1 | Jan. 2010 – Mar. 2011 | Prospective | Elective cardiac surgery with CPB | - | 865 | Serum | NR | > 5 | Non-occlusivemesenteric ischemia | 9% had the outcome. More patients with the outcome had high lactate. Remained in multivariable analysis |
| Lopez-Delgado2013 35 | 1 | Jan. 2004 – Jan. 2009 | Prospective | Cardiac surgery and liver cirrhosis | - | 58 | Arterial  | ICU admission and 24 hour after | NR | Mortality  | 24 hours after was higher in non-survivors, no difference on admission. Did not remain on multivariable analysis |
| Hajjar 2013 36 | 1 | Feb. 2009 – Feb. 2010 | Prospective | Elective cardiac surgery with CPB | Multiple including a number of pre-existing conditions and types of surgery | 502 | Blood | During surgery, ICU arrival, and 6 and 12 hours after | > 3 at 6 hours, > 2 at 24 hours | Complications | Higher lactates in those with complications. Lactate at 6 hours remained associated in multivariable analysis. AUC: 0.72 at 6 hours, AUC: 0.78 at 24 hours |
| Wang 2013 37 | 1 | Jan. 2005 – Dec. 2011 | Retrospective | VA-ECMO after valve surgery | - | 87 | NR | NR | > 12 | Mortality | Peak lactate higher in non-survivors. High lactate associated with mortality in multivariable analysis |
| Jabbari2013 38 | 1 | Aug. – Sept. 2012 | Prospective | Routine cardiac surgery | Surgical complication | 15 | Serum | During (every 30 min) and after (every 6 hours) surgery | NR | Complications | Higher lactate levels in those with complication |
| Laine 2013 39 | 1 | Sept. 2010 – Dec. 2011 | Retrospective | Cardiac surgery with CPB | Combined ScvO2 < 70% andlactate > 2  | 526 | Arterial | Arrival at ICU | > 2/> 4 | LOS, complications, mortality | High lactate associated with LOS and complications but not significantly with mortality. Association with hospital LOS and major complications remained in multivariable analysis |
| Lopez-Delgado 2013 40 | 1 | Jan. 2004 – Jul. 2009 | Retrospective | Cardiac surgery | Heart transplant, pre-operative renal disease and dialysis | 2940 | Arterial | ICU admission and 24 hours after | NR | Acute kidney injury | Higher lactates in those with acute kidney injury. 24 hours lactate remained associated in multivariable analysis |
| Tamayo2013 41,42 | 1 | Jan. 2009 – Jan. 2011 | Prospective | Cardiac valve and/or coronary surgery with CPB | Heart transplant | 909 | Blood | ICU admission | NR | Mortality | Lactate higher in non-survivors. Remained in multiple variable analysis |
| Badreldin 2013 43 | 1 | Jan. 2007 – Dec. 2009 | Prospective | Cardiac surgery | - | 4,054 | Arterial | Highest in first 24 hours after surgery | Multiple cut-offs: 1.8, 6.0, 9.4, and 13.4 | ICU mortality | Increasing mortality with each category. AUC: 0.88. Addition of lactate improved other scoring systems |
| Park2014 44 | 1 | May 2005 – Dec. 2011 | Retrospective | Extra-corporeal life support after cardiac surgery | - | 94 | Serum | Before extra-corporeal life support | >7.9 | Mortality | Higher lactate levels in those that died. Remained in multivariable analysis. Sens. 63%, spec. 68%, AUC: 0.73 for cut-off |
| Park 2014 45 | 1 | May 2005 – Dec. 2012 | Retrospective | Extra-corporeal life support after cardiac surgery | - | 115 | Arterial | Every 2-3 hours | Various | Complications | Higher lactates in those with complications at all time points. Remained in multivariable analysis |
| Ranucci2015 46  | 2 | Jan. 2010 – Dec. 2013 | Retrospective | Cardiac surgery | Heart transplant | 4251 | Arterial | Arrival to ICU | > 4 | Post-operative bleeding | Associated with the outcome. Remained in multivariable analysis |
| Lopez-Delgado2015 47 | 1 | Jan. 2004 – Jan. 2009 | Prospective | Cardiac surgery and liver cirrhosis | - | 51 | Arterial | Admission to ICU and 24 hours after |  | Long-term mortality | 24 hour lactate associated with the outcome. At admission not. Did not remain in multivariable analysis |
| Papadopoulos 2015 48 | 1 | Dec. 2001 – Jun. 2013 | Prospective | Extra-corporeal life support after cardiac surgery  | - | 360 | Serum | NR | > 120 mg/dL | Failure to wean, mortality | Associated with the outcome (unclear which) |
| Rubino2015 49 | 1 | NR | Prospective | Cardiac surgery onCPB with aortic cross-clamping. | Multiple including heart transplant, congenital disease and pre-existing renal failure | 187 | Arterial | Peak during CPB and the first 3 days | > 3 | High lactate, complications, mortality | Included in score that was associated with most of the outcomes |
| Li2015 50 | 1 | Jan. 2011 – Dec. 2012 | Retrospective | VA-ECMO after cardiac surgery | - | 123 | Arterial, serum  | Average and lactate clearance first 6 and 12 hours | NR | Complications, weaning | Both mean and clearance associated with mortality. Remained in multivariable analysis. Only 12 hour associated with weaning |
| Zhang 2015 51 | 1 | Jul. 2012 – Jan. 2014 | Prospective | Cardiac surgery with CPB | Severe complication, prior dialysis | 117 | Serum  | 4-hour intervals for the first 24 hours. Lactate load | 4.4 | Acute kidney injury | Higher in those with the outcome. Remained in multivariable analysis. Initial lactate AUC: 0.63. Sens.: 41%, spec.: 87% for cut-off. Increasing AUC at later time points |
| Saxena 2015 52 | 1 | Jan. 2003 – Jan. 2013 | Retrospective | ECMO after cardiac surgery. > 70 years | - | 45 | NR | Mean and max post-operative | NR | Mortality | Both higher in those that died  |
| Zacharias 2015 53  | 1 | Jul. 2009 – Aug. 2010 | Prospective | Cardiac surgery with CPB | - | 85 | Plasma | 24 hours after surgery | NR | Acute kidney injury | Higher in those with the outcome |
| Hsu 2015 54 | 1 | Jun. 2006 – May 2013 | Retrospective | Heart transplant and lactate > 15 | - | 12 | Arterial  | After surgery | > 15 | Mortality | Return to lactate < 4 associated with time on mechanical ventilation.  |
| Lopez-Delgado 2015 55 | 1 | Jan. 2004 – Dec. 2009 | Prospective | Cardiac surgery | Off-pump surgery, heart transplant and prior liver dysfunction | 2935 | Arterial | ICU admission and 6, 12, and 24 hours later | > 3 | Complication, LOS, in-hospital and long-term mortality | Associated with the outcomes. Higher at all time points in non-survivors (short- and long-term). AUC highest at 24 hours. Changes in lactate similar between groups (no statistics provided)  |
| Youssefi 2015 56 | 1 | Oct. 2011 – Oct. 2013 | Prospective | Cardiac surgery with post-operative “fast track” | Multiple | 451 | NR | Arrival to ICU | NR | Successful fast track management  | Higher lactate in those that failed. Did not remain in multivariable analysis  |
| Andersen2015 57 | 1 | 2002 - 2014 | Retrospective | CABG or valve surgery | No lactate value, off-pump surgery | 1,208 | NR | Within 3 hours of skin closure | > 2> 4 | LOS, complications, mortality | Associated with the outcomes. Remained in multivariable analysis (mortality not analyzed) |
| Ranucci 2015 58 | 1 | Jan. 2010 – Dec. 2013 | Retrospective | Cardiac surgery | Transplant, off-pump | 3,851 | Blood | Arrival in ICU | > 2.1> 6.0 | Complication, mortality | Associated with the outcomes. No multivariable analyses. |
| Jorge-Monjas 2016 59 | 2 | Jan. 2012 – Jan. 2014 and Mar. 2014 – Mar. 2015 | Prospective | CABG and/or valvesurgery with CPB | - | 1551 | NR | During surgery and at arrival to ICU | NR | Acute kidney injury | No difference in lactate during the surgery. Higher in those with the outcome at ICU arrival. Remained in multivariable analysis. Included in score.  |
| Mothes 2016 60 | 1 | Jan. 2005 – Dec. 2012 | Retrospective case-control | Cardiac surgery with CPB | - | 433 | NR | Day 0 and 1 post-operatively | > 3  | Acute mesenteric ischemia (laparotomy) | Higher in cases. Remained in multivariable analysis.  |

a The table provides a brief summarized overview of the different studies. The summary focuses on the reporting and analysis of lactate in the included studies which was often not the primary goal of the study. No formal assessment of the quality of the included studies was performed and the summary results should therefore be interpreted carefully. This table is not meant to be a comprehensive description of the included studies.

b Abbreviations: NR: not reported, CPB: cardiopulmonary bypass, LOS: length of stay, CHF: congestive heart failure, LVEF: left-ventricular ejection fraction, IABP: intraaortic balloon pump, PPV: positive predictive value, NPV: negative predictive value, CABG: coronary artery bypass grafting, AUC: area under the receiver operating characteristics curve, ICU: intensive care unit, sens.: sensitivity, spec: specificity, ECMO: extracorporeal membrane oxygenation, BMI: body mass index, EF: ejection fraction, DO2: Oxygen delivery, Max.: maximum RRT: renal replacement therapy, AF: atrial fibrillation, NYHA: New York Heart Association, EuroSCORE: European system for cardiac operative risk evaluation, VA-ECMO: veno-arterial extracorporeal membrane oxygenation, ScvO2: Central venous oxygen saturation

c All studies were observational cohort studies unless otherwise noted

d All lactates are reported in mmol/L unless otherwise noted

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