

**Table 1:** Studies in the literature that report adequate data regarding postoperative cognitive dysfunction (POCD)/postoperative delirium (POD) presented in chronologically ascending order.

Study	Study type	Type of surgery	Results-Significant variables for outcomes
Monk, 2008 <sup>20</sup>	Prospective	Major noncardiac	POCD was higher at 3 months in elderly patients (p <0.001); Lower educational level, previous cerebral vascular accident POCD at discharge were independent risk factors for POCD at 3 months; POCD at hospital discharge and 3 months were found to increase the mortality risk at 3 months and 12 months respectively
Hudetz, 2009 <sup>63</sup>	Randomised	Cardiac	Ketamine attenuates POCD at 1 week (p <0.001)
Mack, 2009 <sup>64</sup>	Randomised	Vascular	Low dose intraoperative magnesium therapy protects against POCD/POD (P<0.01)
Mathew, 2009 <sup>16</sup>	Randomised	Cardiac	Lidocaine infusions during and after cardiac surgery do not reduce the rate of POCD (p =0.97); Higher doses were independent predictors of POCD (p =0.004)
Mitchell, 2009 <sup>66</sup>	Randomised	Cardiac	Lidocaine was not prove to be neuroprotective
Slater, 2009 <sup>27</sup>	Prospective	Cardiac	Intra-operative cerebral oxygen desaturation is associated with increased risk of POCD/POD (p =0.024)
Steinmetz, 2010 <sup>71</sup>	Prospective	Noncardiac	No significant difference was detected
Evered, 2011 <sup>37</sup>	Prospective	Cardiac Orthopaedic	The incidence of POCD in elderly patients at 7 days (p <0.01); higher after CABG than THJR; independent at 3 months (p =0.24); CV risk factors were not predictive of POCD
Siepe, 2011 <sup>53</sup>	Randomised	Cardiac	Normal perfusion pressures during normothermic CPB (80-90 mmHg) is associated with less early POCD/POD (p =0.017)
Ballard, 2012 <sup>68</sup>	Randomised	Abdominal Orthopaedic	Intraoperative monitoring of anaesthetic depth and cerebral oxygenation may reduce the POCD (p <0.05)
Kline, 2012 <sup>21</sup>	Retrospective	Non-cardiac	Elderly undergoing surgery experience an increased rate of atrophy in hippocampal and gray matter (5-9 months)
Saczynski, 2012 <sup>39</sup>	Prospective	Cardiac	POD is associated with more prolonged cognitive decline within 12 months after cardiac surgery
Chan, 2013 <sup>69</sup>	Randomized double blind	Major noncardiac	BIS-guided anesthesia decreased the risk of POCD at 3 months (10.2% vs. 14.7%, p =0.025)
Krüger, 2013 <sup>55</sup>	GERAADA registry	Acute Aortic Dissection type A	Steroid administration may be associated with improved neurological outcomes
Lamy, 2013 <sup>43</sup>	Prospective	Cardiac	At 1 year after CABG there was no significant difference between off-pump and on-pump CABG to the neurocognitive function
Mathew, 2013 <sup>65</sup>	Randomised	Cardiac	Magnesium administered during and after cardiac surgery does not reduce POCD (p =0.93)
Mu, 2013 <sup>40</sup>	Prospective	Cardiac	High serum cortisol level in 1 <sup>st</sup> postoperative morning associated with increased risk of cognitive dysfunction 7 days after CABG (p =0.003)
Radtke, 2013 <sup>70</sup>	Prospective	Noncardiac	Intraoperative neuromonitoring is associated with a lower incidence of POD (p =0.036)
Sauër, 2013 <sup>5</sup>	Randomised	Cardiac	At 7.5 years follow-up off-pump CABG had a similar or even better cognitive performance compared PCI (p <0.01)
Colton, 2014 <sup>56</sup>	Retrospective	-	Propofol does not have long-term effects on intracranial hypertension
Ellard, 2014 <sup>33</sup>	Retrospective	Vascular	POD after vascular anesthesia is similar with regional or general anesthesia (p =0.56)
Fang, 2014 <sup>28</sup>	Prospective	Microvascular decompression	Higher doses of dexamethasone increases the incidence of early POCD
Kok, 2014 <sup>50</sup>	Pilot study	Cardiac	No significant difference in cerebral oxygenation; CPB identified as independent risk factor for development of late cognitive dysfunction (p =0.027)
Krenk, 2014 <sup>36</sup>	Prospective	Orthopaedic	The incidence of early, but not late, POCD after total hip and knee replacement seems to be lower after a fast-track approach
Mahajan, 2014 <sup>61</sup>	Randomised	Neurosurgery	Neuroprotection with propofol at the time of clipping during aneurysm surgery was not adequate
Ottens, 2014 <sup>29</sup>	Randomised	Cardiac	Treatment group did not differ in the incidence of POCD 1 (p =0.09) or 12 (p =0.24) months postoperatively
Papadopoulos, 2014 <sup>67</sup>	Randomised	Orthopaedic	Postoperative ondansetron administration seems to protect; might improve cognitive function in pts undergoing hip fracture surgery under GA
Saporito, 2014 <sup>57</sup>	Prospective	ICU +/- major	Early POD is very common after major surgery, even without known risk factors (p <0.02)
Shi, 2014 <sup>39</sup>	Animal study	-	Propofol exerts neuroprotection against ischemic brain damage
Wang, 2014 <sup>62</sup>	Randomised	-	Propofol-Dexametomidine combination exerts a stronger neuroprotection against ischemia reperfusion
Zhang, 2014 <sup>60</sup>	Animal study	-	Propofol has a neuroprotective effect on hippocampal injury induced by hypoxia
Zhu, 2014 <sup>30</sup>	Prospective	Orthopaedic	Perioperative blood transfusion >3 RBCs = independent risk factor for POCD in aged patients following total hip replacement surgery (p <0.05)
Hudetz, 2015 <sup>47</sup>	Randomised	Cardiac	RIPOC prevented deterioration of short-term POCD (p <0.05) but there were no results in POD (p =0.54)
Tachibana, 2015 <sup>22</sup>	Pilot study	Major surgery	Elderly patients undergoing desflurane anesthesia have significant better quality of emergence (p <0.05)
Cereghetti, 2017 <sup>31</sup>	Retrospective	Cardiac	Known risk factors for POD are also predictive of prolonged duration of POD
Chen, 2017 <sup>32</sup>	Randomized	Orthopaedic	GA is associated with higher cognitive decline compared to combined general anaesthesia (p =0.005)
Del Felice, 2016 <sup>54</sup>	Prospective	Cardiac	A decline in hematocrits level <12 % represents a threshold for cognitive decline
Dokkedal, 2016 <sup>24</sup>	Prospective	All types	A statistically significant decrease (-0.27; 95% CI, -0.48 to 0.06) in cognitive function was present in twins with at least one major surgery
Micha, 2016 <sup>12</sup>	Randomised	Major noncardiac	Sevoflurane has a negative influence on postoperative cognition
Rappold, 2016 <sup>23</sup>	Prospective	Noncardiac	Postoperative cognitive decline 1 month after surgery was associated with higher plasma concentrations of the biomarker GFAP
Tzimas, 2016 <sup>25</sup>	Prospective	Orthopaedic	Repeated exposure of elderly patients to GA might lead to prolonged cognitive impairment
Abrahamov, 2017 <sup>48</sup>	Prospective	Cardiac	The location and intensity BBB disruption is correlated with POCD
Glumac, 2017 <sup>49</sup>	Randomised	Cardiac	Preoperative dexamethasone reduced the inflammatory response and the risk of early POCD
Kok, 2017 <sup>42</sup>	Prospective	Cardiac	Postoperative cognitive dysfunction could be solely attributable to CPB
Knipp, 2017 <sup>52</sup>	Prospective	Cardiac	Silent brain infarcts did not impact early or late cognitive performance
Todd, 2017 <sup>17</sup>	Prospective	Orthopaedic	Older people with sleep disruption are at higher risk of POD
Tzimas, 2018 <sup>13</sup>	Randomised	Orthopaedic	The choice of anesthesia does not influence the emergence of POCD in elderly patients undergoing hip fracture surgery
Zhang, 2018 <sup>19</sup>	Sub-analysis Randomised	Cancer surgery	Vitamin D deficiency increases the risk of early POCD

POCD: postoperative cognitive dysfunction, CABG: coronary artery bypass grafting, THJR: total hip joint replacement, CV: cardiovascular, POD: postoperative delirium, PCI: percutaneous coronary intervention, CPB: cardiopulmonary bypass, RBCs: red blood cells, GFAP: glial fibrillary acid protein.