

普外科肿瘤患者围术期神经认知障碍的研究进展

李子毅, 王 舟*

山东大学齐鲁医院麻醉科, 山东 济南

收稿日期: 2025年10月11日; 录用日期: 2025年11月4日; 发布日期: 2025年11月12日

摘 要

围术期神经认知障碍(PND)是普外科肿瘤患者常见的围术期神经系统并发症, 会延长住院时间、增加并发症和长期认知障碍的风险, 最终影响患者预后及转归, 已成为该类患者围术期管理的重点问题。本文从围术期神经认知障碍的流行病学、发病机制、危险因素、预防以及其对普外科肿瘤患者预后的影响等方面进行综述, 为麻醉科和普外科医师提供有临床价值的参考意见, 并为后续研究提供参考。

关键词

围术期神经认知障碍, 术后谵妄, 术后神经认知障碍, 肿瘤

Progress on Perioperative Neurocognitive Disorders in Patients with General Surgery Tumors

Ziyi Li, Zhou Wang*

Department of Anesthesiology, Qilu Hospital of Shandong University, Jinan Shandong

Received: October 11, 2025; accepted: November 4, 2025; published: November 12, 2025

Abstract

Perioperative Neurocognitive Disorders (PND) represent a prevalent neurological complication in general surgical oncology patients, which may prolong hospitalization, increase the risk of complications and long-term cognitive impairment, ultimately affecting patient prognosis and outcomes.

*通讯作者。

文章引用: 李子毅, 王舟. 普外科肿瘤患者围术期神经认知障碍的研究进展[J]. 临床医学进展, 2025, 15(11): 981-988.
DOI: 10.12677/acm.2025.15113182

Consequently, PND has emerged as a critical issue in perioperative management for this patient population. This article provides a comprehensive review of PND from multiple perspectives, including epidemiology, pathogenesis, risk factors, prevention strategies, and its impact on the prognosis of general surgical oncology patients. The review aims to offer clinically valuable insights for anesthesiologists and general surgeons, while also serving as a reference for subsequent research endeavors.

Keywords

Perioperative Neurocognitive Disorders, Postoperative Delirium, Postoperative Neurocognitive Disorders, Tumor

Copyright © 2025 by author(s) and Hans Publishers Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

1. 引言

围术期神经认知障碍(perioperative neurocognitive disorder, PND)是围术期最常见的神经系统并发症之一,根据发生时间可分为五种:1)术前已存在的认知功能障碍;2)术后谵妄(postoperative delirium, POD)即术后一周内或出院前发生的认知功能障碍;3)延迟神经认知恢复(delayed neurocognitive recovery, dNCR)即术后30天内诊断出的认知功能障碍;4)术后认知功能障碍(postoperative cognitive dysfunction, POCD)即术后30天到12个月发生的认知功能障碍;5)术后认知功能减退即术后12个月后诊断的认知功能障碍[1][2]。PND的发生与手术类型、病人自身情况等多种因素相关[3][4],而普外科肿瘤患者因患者自身情况、手术相关因素等,发生PND风险明显升高,给患者家庭以及社会带来了严重的负担[5]。本文系统检索了PubMed、Web of Science、中国知网(CNKI)和万方数据库,检索时间范围为2018年1月至2024年12月,检索关键词包括:“围术期神经认知障碍”、“术后谵妄”、“术后认知功能障碍”、“肿瘤手术”、“普外科”、“PND”、“POD”、“POCD”等中英文术语,并采用布尔逻辑运算符进行组合检索,针对普外科肿瘤患者发生PND的危险因素、预后影响和干预措施进行综述,为临床医生提供参考。

2. PND的流行病学、发病机制、危险因素

2.1. 流行病学

研究发现,肿瘤患者行外科手术PND发生率为8%~23% [6] [7],且恶性肿瘤可能与PND发生率增高有关[8]。

2.2. 发病机制

到目前为止,PND的准确发病机制仍在不断研究中,但可能的机制如炎症已被许多研究涉及。一项针对643名结肠癌患者的临床研究发现,发生PND的患者术后第一天炎症标志物升高,如C反应蛋白升高[9]。Brattinga等人通过对65岁以上的老年肿瘤患者的研究证实,术后中性粒细胞明胶酶相关脂钙素(NGAL)和IL-10的升高与PND的发病率增加有关[10]。肠道菌群是PND发病机制中的一个新兴因素,最新研究发现,肠道菌群可能通过改变对氧化应激的耐受性来影响胃癌患者PND的发生[11]。此外,研究发现机械肠道准备(mechanical bowel preparation, MBP)不仅改变了胃癌患者肠道菌群组成,而且增加了PND的发生率,在MBP改变的肠道菌群中,拟杆菌属和细微杆菌属可能是PND的危险因素[12]。

2.3. 危险因素

普外科肿瘤患者发生 PND 的危险因素很多, 可分为术前、术中、术后因素。

PND 的术前预测因素包括高龄、男性、文化水平低、焦虑抑郁、缺乏社会支持、睡眠障碍等[13]-[16]。普外科肿瘤患者与其他患者相比, 营养状况往往更差[17], 更多患者处于术前衰弱状态[18], 这也是 PND 发生的危险因素。最新研究发现, 术前血清白蛋白以及术前血红蛋白是影响老年原发性肝癌患者术后谵妄发生的重要因素[19], 这可能是因为术前血红蛋白及血清白蛋白水平的降低提示患者存在慢性贫血、营养状况差、机体免疫功能低下, 因此在手术过程中, 机体对手术的耐受性更差, 发生 PND 的风险越高[20]。此外, 患者在家使用药物, 如抗胆碱能药和苯二氮卓类药物, 都被认为是癌症手术患者发生 PND 的危险因素[21]。

许多临床研究探索了术中与 PND 发生率增加相关的因素。台湾一项针对开腹手术的老年肿瘤患者的研究表明, 手术时间越长、手术创伤越大, 患者发生 PND 的风险更高[22]。最新研究发现, 对于腹腔镜肝脏肿瘤切除术患者, 术中脑氧饱和度 rSO_2 下降程度增大是其发生 PND 的独立危险因素[23], 这可能是因为腹腔镜肝部分切除术常采用控制性低中心静脉压(CLCVP)及肝血流阻断技术减少术中失血, 但这导致大脑等重要组织及器官缺血低氧损伤、脑氧代谢不平衡而影响病人认知功能[24]。

一项针对老年人腹腔镜胃切除术的研究分析了 PND 发生的术后危险因素, 并建立了 nomogram 预测模型。该研究证实术后与癌症患者 PND 风险增加相关的因素包括 ICU 住院时间延长、白蛋白/纤维蛋白原比值升高、中性粒细胞/淋巴细胞比值升高[25]。

3. PND 的预防

普外科肿瘤患者 PND 的防治应贯穿整个围术期, 形成一个以“风险评估-精准干预-长期随访”为核心的闭环管理模式。本部分将从非药物与药物两个维度, 系统阐述具有循证医学支持的防治策略。

3.1. 非药物预防: 构建围术期脑健康防护体系

非药物干预是预防 PND 的基石, 其核心在于通过多学科协作, 优化患者全身状态与神经认知环境。

3.1.1. 术前预康复与全面评估

建议组建包括外科、麻醉、老年、营养、康复在内的多学科团队。对高龄、衰弱、营养不良、存在焦虑抑郁或认知功能下降的患者进行重点筛查与干预。措施包括: ① 营养支持: 纠正低白蛋白血症与贫血; ② 体能锻炼: 指导进行术前适度锻炼, 增强生理储备; ③ 认知预康复: 进行认知训练, 并管理焦虑情绪。研究表明, 对结直肠癌衰弱老年人实施完善的老年评估与共管, 可显著降低 PND 风险[26]。

3.1.2. 术中脑功能监测与保护

脑氧饱和度监测应被视为高危患者的重要监测手段。对于腹腔镜肝切除术等可能影响脑灌注的手术, 实施以局部脑氧饱和度为目标导向的管理策略, 避免其大幅下降, 已被证实能有效降低 PND 发生率[23][27]。

3.1.3. 术后早期强化康复(ERAS)

① 早期活动: 鼓励并协助患者术后尽早下床活动, 打破卧床-功能下降的恶性循环[28][29]。② 睡眠管理: 优化病房环境, 减少夜间灯光与噪音干扰, 促进睡眠周期恢复。③ 疼痛管理: 采用多模式镇痛, 减少阿片类药物用量, 避免其导致的镇静与谵妄。

3.2. 麻醉与药物预防: 精准靶控干预

在非药物干预基础上, 合理运用药物与麻醉技术可进一步降低 PND 风险。

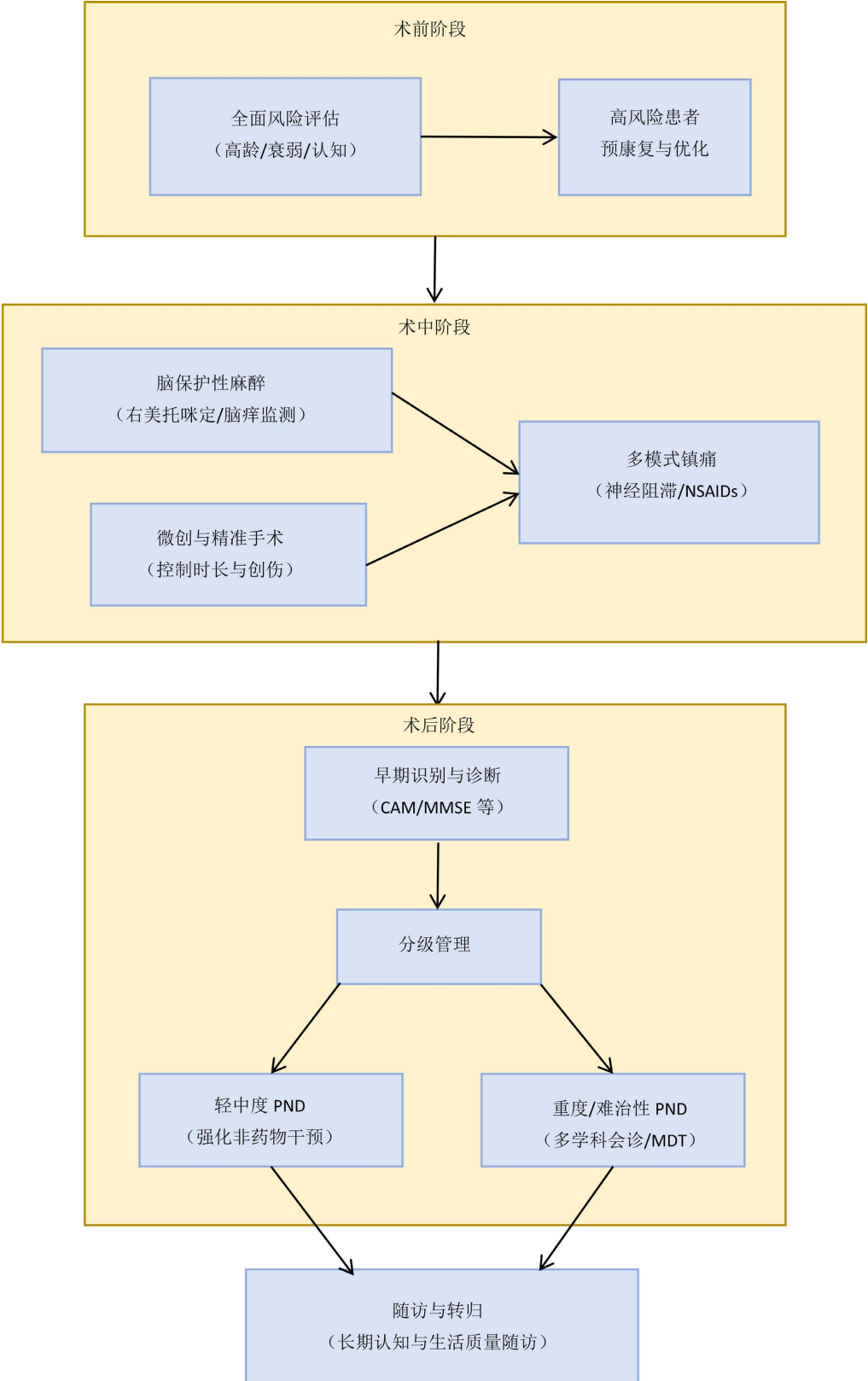


Figure 1. Clinical pathway for PND management in surgical oncology patients
图 1. 普外科肿瘤患者围术期神经认知障碍(PND)综合防治临床路径

3.2.1. 麻醉药物选择

右美托咪定因其具有抗交感、镇静镇痛且无呼吸抑制的特性, 成为研究热点。术中应用可通过降低炎症介质(如 IL-6)水平、调节 PI3K/AKT 等神经保护通路, 显著降低胃癌、结直肠癌患者 PND 发生率[30]-[32]。关于全凭静脉麻醉(丙泊酚)与吸入麻醉(七氟烷)的优劣, 现有证据存在争议[27][33][34]。临床决策应个体化, 但对于高危老年患者, 可考虑优先采用以丙泊酚为基础的麻醉方案。

3.2.2. 多模式镇痛

① 神经阻滞: 采用右美托咪定复合罗哌卡行腹横肌平面(TAP)阻滞, 在提供优良镇痛的同时, 其本身即被证明是降低 PND 的独立保护因素[35]。② 非甾体抗炎药: 如氟比洛芬酯, 在改善术后镇痛效果的同时, 可能通过改善脑氧饱和度而发挥脑保护作用[36]。③ 阿片药物节俭: 采用手术体积描记指数(SPI)等技术指导阿片类药物精确使用, 可减少术后躁动等不良事件, 从而降低 PND 风险[37]。

3.2.3. 其他药物探索

术前预防性联合使用苏沃雷生和雷美替恩显示出降低 PND 风险的潜力[38], 但其广泛应用仍需更多证据支持。

4. PND 对普外科肿瘤患者预后的影响

越来越多的研究强调了肿瘤患者与 PND 相关的各种不良后果, 包括死亡率上升、住院时间延长、增加医疗成本等。有研究表明, 许多患者罹患 PND 后, 自理能力下降甚至丧失自理能力, 这也增添了其家庭及社会负担[39][40]。此外, 还有研究发现, 癌症患者 PND 的发生与 30 天、90 天再入院率增加等不良结局相关[41], 这可能与他们出院后无法正确理解遵循医嘱、不能正确进行康复训练、身体功能恢复受影响相关。

5. 小结与展望

普外科肿瘤患者的 PND 管理已从单一的并发症处理, 发展为关乎患者远期生活质量的系统性工程。通过本文综述, 我们提出以下整合性临床管理路径(见图 1), 旨在为临床医师提供一个清晰、可操作的实践框架。

然而, 要将 PND 的防治提升至新高度, 仍有诸多关键科学问题亟待深入探索: 1) 机制研究的深度与转化: 当前对 PND 发病机制的理解仍多集中于炎症反应, 未来研究需整合神经科学、免疫学及肿瘤生物学, 阐明从外周炎症到中枢认知功能损害的具体信号通路, 并寻找可用于早期诊断和靶向干预的关键分子靶点; 2) 精准风险预测模型的构建: 现有的风险因素列表虽不断延长, 但缺乏能够整合患者术前认知储备、遗传易感性、特定肿瘤类型、手术创伤及围术期管理细节的高精度、个体化预测模型。如何利用多组学数据、脑功能影像及人工智能技术, 构建适用于中国人群的普外科肿瘤患者 PND 风险预测工具, 是实现早期精准识别的关键; 3) 预防策略的优化与循证: 如何根据患者不同的风险谱, 制定个体化的、最优化的多模式预防方案(包括药物与非药物)。解决以上问题, 需要设计严谨的前瞻性队列研究和多中心随机对照试验, 并建立完善的长期随访体系。这不仅是麻醉学和外科领域的任务, 更需要神经科学、老年医学、肿瘤学及生物信息学等多学科的交叉合作, 共同攻克 PND 这一难题, 最终改善普外科肿瘤患者的整体预后。

参考文献

- [1] Evered, L., Silbert, B., Knopman, D.S., Scott, D.A., DeKosky, S.T., Rasmussen, L.S., *et al.* (2018) Recommendations for the Nomenclature of Cognitive Change Associated with Anaesthesia and Surgery—2018. *Anesthesiology*, **129**, 872-

879. <https://doi.org/10.1097/aln.0000000000002334>
- [2] 翟菲菲, 黄宇光. 围术期神经认知障碍: 从术后到术前, 从临床指标到生物学指标[J]. 临床麻醉学杂志, 2019, 35(4): 317-318.
- [3] O'Brien, H., Mohan, H., Hare, C.O., Reynolds, J.V. and Kenny, R.A. (2017) Mind over Matter? The Hidden Epidemic of Cognitive Dysfunction in the Older Surgical Patient. *Annals of Surgery*, **265**, 677-691. <https://doi.org/10.1097/sla.0000000000001900>
- [4] Evered, L., Atkins, K., Silbert, B. and Scott, D.A. (2022) Acute Peri-Operative Neurocognitive Disorders: A Narrative Review. *Anaesthesia*, **77**, 34-42. <https://doi.org/10.1111/anae.15613>
- [5] Tjeertes, E.K.M., van Fessem, J.M.K., Mattace-Raso, F.U.S., Hoofwijk, A.G.M., Stolker, R.J. and Hoeks, S.E. (2020) Influence of Frailty on Outcome in Older Patients Undergoing Non-Cardiac Surgery—A Systematic Review and Meta-analysis. *Aging and disease*, **11**, 1276-1290. <https://doi.org/10.14336/ad.2019.1024>
- [6] Ho, M., Nealon, J., Igwe, E., Traynor, V., Chang, H., Chen, K., et al. (2021) Postoperative Delirium in Older Patients: A Systematic Review of Assessment and Incidence of Postoperative Delirium. *Worldviews on Evidence-Based Nursing*, **18**, 290-301. <https://doi.org/10.1111/wvn.12536>
- [7] Zhao, B., Ji, H., Xu, C., Li, D., Xing, Z., Liu, B., et al. (2023) Incidence and Risk Factors of Postoperative Delirium after Pancreatic Cancer Surgery: A Retrospective Study. *Surgery Today*, **53**, 736-742. <https://doi.org/10.1007/s00595-022-02614-4>
- [8] Ke, Y., Chew, S., Seet, E., Wong, W.Y., Lim, V., Chua, N., et al. (2023) Risk Factors of Post-Anaesthesia Care Unit Delirium in Patients Undergoing Non-Cardiac Surgery in Singapore. *Singapore Medical Journal*, **64**, 728-731. <https://doi.org/10.11622/smedj.2021129>
- [9] Sun, Y., Peng, H. and Wu, T. (2023) Postoperative C-Reactive Protein Predicts Postoperative Delirium in Colorectal Cancer Following Surgery. *Clinical Interventions in Aging*, **18**, 559-570. <https://doi.org/10.2147/cia.s387117>
- [10] Brattinga, B., Plas, M., Spikman, J.M., Rutgers, A., de Haan, J.J., Absalom, A.R., et al. (2022) The Association between the Inflammatory Response Following Surgery and Post-Operative Delirium in Older Oncological Patients: A Prospective Cohort Study. *Age and Ageing*, **51**, afab237. <https://doi.org/10.1093/ageing/afab237>
- [11] Liu, H. and Liu, X. (2022) Response: Commentary: Preoperative Status of Gut Microbiota Predicts Postoperative Delirium in Patients with Gastric Cancer. *Frontiers in Psychiatry*, **13**, Article ID: 852269. <https://doi.org/10.3389/fpsy.2022.991290>
- [12] Yang, Z., Tong, C., Qian, X., Wang, H. and Wang, Y. (2022) Mechanical Bowel Preparation Is a Risk Factor for Post-operative Delirium as It Alters the Gut Microbiota Composition: A Prospective Randomized Single-Center Study. *Frontiers in Aging Neuroscience*, **14**, Article ID: 847610. <https://doi.org/10.3389/fnagi.2022.847610>
- [13] Li, Y., Li, Z., Lv, Q., Gu, Y., Qi, Y., Li, J., et al. (2024) Prevalence and Risk Factors of Postoperative Delirium in Tumor Patients after Free Flap Reconstruction: A Systematic Review and Meta-Analysis of Case-Control Studies. *Surgery*, **176**, 906-917. <https://doi.org/10.1016/j.surg.2024.05.009>
- [14] Liu, X., Huangfu, Z., Zhang, X. and Ma, T. (2025) Global Research Trends in Postoperative Delirium and Its Risk Factors: A Bibliometric and Visual Analysis. *Journal of PeriAnesthesia Nursing*, **40**, 400-414. <https://doi.org/10.1016/j.jopan.2024.04.002>
- [15] Paunekar, S. and Chakole, V. (2024) Postoperative Delirium and Neurocognitive Disorders: A Comprehensive Review of Pathophysiology, Risk Factors, and Management Strategies. *Cureus*, **16**, e68492. <https://doi.org/10.7759/cureus.68492>
- [16] Suzuki, R., Nakanishi, A., Masuya, M., Fukuroku, K., Taneda, Y. and Matsuura, Y. (2025) Risk Factors for Postoperative Delirium in Patients Undergoing Orthopedic Procedures: A Systematic Review and Meta-Analysis. *PLOS ONE*, **20**, e0321025. <https://doi.org/10.1371/journal.pone.0321025>
- [17] Yang, Z., Wang, X., Yang, L., Fang, C., Gu, X. and Guo, H. (2020) Prevalence and Risk Factors for Postoperative Delirium in Patients with Colorectal Carcinoma: A Systematic Review and Meta-Analysis. *International Journal of Colorectal Disease*, **35**, 547-557. <https://doi.org/10.1007/s00384-020-03505-1>
- [18] Tian, J., Hao, X., Cao, F., Liu, J., Li, Y., Guo, Y., et al. (2023) Preoperative Frailty Assessment Predicts Postoperative Mortality, Delirium and Pneumonia in Elderly Lung Cancer Patients: A Retrospective Cohort Study. *Annals of Surgical Oncology*, **30**, 7442-7451. <https://doi.org/10.1245/s10434-023-13696-w>
- [19] 马垚, 李婷, 张秋实, 等. 60 岁以上原发性肝癌患者术后谵妄发生风险预测模型的构建及验证[J]. 临床肝胆病杂志, 2024, 40(9): 1816-1821.
- [20] Taylor, J., Payne, T., Casey, C., Kunkel, D., Parker, M., Rivera, C., et al. (2023) Sevoflurane Dose and Postoperative Delirium: A Prospective Cohort Analysis. *British Journal of Anaesthesia*, **130**, e289-e297. <https://doi.org/10.1016/j.bja.2022.08.022>

- [21] Mueller, A., Spies, C.D., Eckardt, R., Weiss, B., Pohrt, A., Wernecke, K., *et al.* (2020) Anticholinergic Burden of Long-Term Medication Is an Independent Risk Factor for the Development of Postoperative Delirium: A Clinical Trial. *Journal of Clinical Anesthesia*, **61**, Article 109632. <https://doi.org/10.1016/j.jclinane.2019.109632>
- [22] Lai, C., Liu, K., Tsai, C., Hsu, J., Hsueh, S., Hung, C., *et al.* (2023) Risk Factors and Effect of Postoperative Delirium on Adverse Surgical Outcomes in Older Adults after Elective Abdominal Cancer Surgery in Taiwan. *Asian Journal of Surgery*, **46**, 1199-1206. <https://doi.org/10.1016/j.asjsur.2022.08.079>
- [23] 闫红, 辛艳, 侯念果, 等. 老年腹腔镜肝部分切除术后认知功能障碍的影响因素[J]. 青岛大学学报(医学版), 2023, 59(3): 425-429.
- [24] Dheer, A., Jain, V., Kushwah, N., Kumar, R., Prasad, D. and Singh, S.B. (2018) Temporal and Spatial Changes in Glial Cells during Chronic Hypobaric Hypoxia: Role in Neurodegeneration. *Neuroscience*, **383**, 235-246. <https://doi.org/10.1016/j.neuroscience.2018.04.026>
- [25] Chen, J., Ji, X. and Xing, H. (2022) Risk Factors and a Nomogram Model for Postoperative Delirium in Elderly Gastric Cancer Patients after Laparoscopic Gastrectomy. *World Journal of Surgical Oncology*, **20**, Article No. 315. <https://doi.org/10.1186/s12957-022-02793-x>
- [26] Rostoft, S. and Hamaker, M.E. (2020) Basic Geriatric Principles for Colorectal Surgeons: How to Optimize Assessment and Care of Older Patients in the Perioperative Period. *European Journal of Surgical Oncology*, **46**, 310-315. <https://doi.org/10.1016/j.ejso.2019.07.027>
- [27] 周兴, 杨吉安, 彭凡凡, 等. 局部脑氧饱和度监测目标导向管理对行腹腔镜肝切除术老年肝癌患者术后认知功能的影响[J]. 山东医药, 2025, 65(4): 78-82.
- [28] Takahashi, N., Hiraki, A., Kawahara, K., Nagata, M., Yoshida, R., Matsuoka, Y., *et al.* (2021) Postoperative Delirium in Patients Undergoing Tumor Resection with Reconstructive Surgery for Oral Cancer. *Molecular and Clinical Oncology*, **14**, Article No. 60. <https://doi.org/10.3892/mco.2021.2222>
- [29] Yuan, Y., Gu, Q., Zhu, M., Zhang, Y. and Lan, M. (2023) Frailty-Originated Early Rehabilitation Reduces Postoperative Delirium in Brain Tumor Patients: Results from a Prospective Randomized Study. *Asia-Pacific Journal of Oncology Nursing*, **10**, Article 100263. <https://doi.org/10.1016/j.apjon.2023.100263>
- [30] Ma, X., Lv, S., Wei, S., Mao, B., Zhao, X., Jiang, X., *et al.* (2023) Influences of Dexmedetomidine on Stress Responses and Postoperative Cognitive and Coagulation Functions in Patients Undergoing Radical Gastrectomy under General Anesthesia. *World Journal of Gastrointestinal Surgery*, **15**, 1169-1177. <https://doi.org/10.4240/wjgs.v15.i6.1169>
- [31] Wang, Z., Shen, Z., Wang, H., Zhang, L. and Dong, R. (2020) Effect of Dexmedetomidine on the Cognitive Function of Patients Undergoing Gastric Cancer Surgery by Regulating the PI3K/AKT Signaling Pathway. *Oncology Letters*, **19**, 1151-1156. <https://doi.org/10.3892/ol.2019.11224>
- [32] Zhang, J., Liu, G., Zhang, F., Fang, H., Zhang, D., Liu, S., *et al.* (2019) Analysis of Postoperative Cognitive Dysfunction and Influencing Factors of Dexmedetomidine Anesthesia in Elderly Patients with Colorectal Cancer. *Oncology Letters*, **18**, 3058-3064. <https://doi.org/10.3892/ol.2019.10611>
- [33] Ding, Y., Yu, J., Cui, F. and Li, J. (2022) Comparison of Intravenous and Inhalational Anesthetic on Postoperative Cognitive Outcomes in Elderly Patients Undergoing Cancer Surgery: Systematic Review and Meta-Analysis. *Journal of PeriAnesthesia Nursing*, **37**, 683-690. <https://doi.org/10.1016/j.jopan.2021.11.017>
- [34] 刘双双. 吸入不同时长七氟烷复合丙泊酚麻醉对老年患者围术期神经认知障碍的影响[D]: [硕士学位论文]. 秦皇岛: 华北理工大学, 2020.
- [35] Yang, L., Xiong, R., Chen, X., Wang, S. and Yu, D. (2024) The Influence of Dexmedetomidine Added to Ropivacaine for Transversus Abdominis Plane Block on Perioperative Neurocognitive Disorders after Radical Colorectal Cancer Surgery: Randomized, Double-Blind, Controlled Trial. *BMC Anesthesiology*, **24**, Article No. 186. <https://doi.org/10.1186/s12871-024-02569-8>
- [36] Shen, L., Chen, J., Yang, X., Hu, J., Gao, W., Chai, X., *et al.* (2022) Flurbiprofen Used in One-Lung Ventilation Improves Intraoperative Regional Cerebral Oxygen Saturation and Reduces the Incidence of Postoperative Delirium. *Frontiers in Psychiatry*, **13**, Article ID: 889637. <https://doi.org/10.3389/fpsy.2022.889637>
- [37] Won, Y.J., Oh, S.K., Lim, B.G., Kim, Y.S., Lee, D.Y. and Lee, J.H. (2023) Effect of Surgical Pleth Index-Guided Remifentanyl Administration on Perioperative Outcomes in Elderly Patients: A Prospective Randomized Controlled Trial. *BMC Anesthesiology*, **23**, Article No. 57. <https://doi.org/10.1186/s12871-023-02011-5>
- [38] Ikeuchi, S., Tanaka, R., Sugiura, T., Shinsato, K., Wakabayashi, A., Sato, J., *et al.* (2023) Efficacy of Combined Use of Suvorexant and Ramelteon in Preventing Postoperative Delirium: A Retrospective Comparative Study. *Journal of Pharmaceutical Health Care and Sciences*, **9**, Article No. 42. <https://doi.org/10.1186/s40780-023-00311-z>
- [39] O'Hanlon, S., Baxter, M. and Hosie, A. (2021) Postoperative Delirium in Older Patients with Cancer: The Role of Psychological Distress and Social Support. *Current Opinion in Supportive & Palliative Care*, **16**, 38-47.

- <https://doi.org/10.1097/spc.0000000000000588>
- [40] Gearhart, S.L., Do, E.M., Owodunni, O., Gabre-Kidan, A.A. and Magnuson, T. (2020) Loss of Independence in Older Patients after Operation for Colorectal Cancer. *Journal of the American College of Surgeons*, **230**, 573-582. <https://doi.org/10.1016/j.jamcollsurg.2019.12.021>
- [41] Katayama, E.S., Stecko, H., Woldesenbet, S., Khalil, M., Munir, M.M., Endo, Y., *et al.* (2024) The Role of Delirium on Short- and Long-Term Postoperative Outcomes Following Major Gastrointestinal Surgery for Cancer. *Annals of Surgical Oncology*, **31**, 5232-5239. <https://doi.org/10.1245/s10434-024-15358-x>