

基于液体活检技术的多癌种联合筛查专家共识(2025 版)

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【摘要】 恶性肿瘤是全球重大公共卫生挑战, 筛查是降低其死亡率的关键手段。然而, 目前仅少数癌种有适宜的筛查方法, 且传统单癌筛查方法存在侵入性强、准确性低、依从性差等弊端。基于液体活检技术的多癌种早期检测(MCED), 通过检测血液等体液中的细胞游离 DNA、细胞游离 RNA、蛋白质和代谢物等标志物, 实现了无创、高效的多癌种联合早期检测, 显著拓展了可筛查癌种范围及筛查人群覆盖率, 展现出改善当前癌症筛查策略的巨大潜力。基于液体活检技术的多癌种联合筛查专家共识(2025 版)系统梳理了基于液体活检技术的 MCED 进展、标志物选择与检测技术、癌种选择、研究设计与临床效用评估以及实施路径等内容, 旨在为 MCED 的深入研究与广泛应用提供科学指导, 推动恶性肿瘤筛查策略的持续优化。

【关键词】 恶性肿瘤; 液体活检; 多癌种联合筛查; 肿瘤标志物; 专家共识

实践指南注册: 国际实践指南注册与透明化平台(PREPARE-2025CN680)

基金项目: 国家自然科学基金(82273721); 国家重点研发计划(2023YFC2413200); 中国医学科学院医学与健康科技创新工程(2025-I2M-KJ-007)

Expert consensus on liquid biopsy-based multi-cancer early detection (2025 edition)

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DOI: 10.3760/cma.j.cn112152-20250605-00257

收稿日期 2025-06-05 本文编辑 殷宝侠

引用本文: 陈万青, 陈可欣, 贺宇彤, 等. 基于液体活检技术的多癌种联合筛查专家共识(2025 版)[J]. 中华
肿瘤杂志, 2025, 47(7): 558-574. DOI: 10.3760/cma.j.cn112152-20250605-00257.



完善的知情同意流程,确保受检者充分理解检测的局限性和潜在风险。

专家共识意见 11:多癌筛查具体适用人群需综合考量癌种类型、检测性能等多维度因素,携带多癌高风险因素(吸烟、饮酒、肥胖等)的人群可更为积极地考虑筛查;MCED 技术虽有潜力,但需更多临床研究来验证其实际获益。未来投入使用时,可作为现有标准筛查方案的补充,与现有方案协同开展恶性肿瘤筛查(专家推荐等级:强推荐)。

八、小结与展望

基于液体活检技术的 MCED 作为恶性肿瘤筛查领域的重要突破,正在重塑传统的恶性肿瘤筛查模式。本专家共识系统地阐述了 MCED 在多癌种联合筛查中所发挥的关键作用,梳理了其通过无创方式检测 cfDNA、cfRNA、蛋白质和代谢物等生物标志物的技术优势以及开发和应用流程,为克服传统单癌筛查的局限性指明了新的研究方向。随着研究的不断深入和技术的持续进步,MCED 有望在早期恶性肿瘤检测性能方面得到进一步优化与提升,应用成本得到更好的控制,与现有筛查手段形成优势互补的协同筛查模式,最终实现更高效、更精准的恶性肿瘤早诊早治体系,为全球恶性肿瘤负担的降低作出重要贡献。但这一目标的实现仍需科研人员、临床医师、监管机构和企业等多方面的共同努力和协同合作。

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利益冲突 所有作者声明无利益冲突

致谢 吴晓晖(上海小荷医学检验实验室有限公司)在本共识的多癌筛查标志物分析 AI 算法及人工智能医疗器械、数据质量等方面提供重要参考意见

参 考 文 献

- Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2024, 4(3):229-263. DOI:10.3322/caac.21834.
- Han BF, Zheng RS, Zeng HM, et al. Cancer incidence and mortality in China, 2022[J]. J Natl Cancer Cent, 2024, 4(1):47-53. DOI:10.1016/j.jncc.2024.01.006.
- Qi JL, Li ML, Wang LJ, et al. National and subnational trends in cancer burden in China, 2005-20: an analysis of national mortality surveillance data[J]. Lancet Public Health, 2023, 8(12):e943-e955. DOI:10.1016/S2468-2667(23)00211-6.
- National Lung Screening Trial Research Team, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening[J]. N Engl J Med, 2011, 365(5):395-409. DOI:10.1056/NEJMoa1102873.
- Mittra I, Mishra GA, Dikshit RP, et al. Effect of screening by clinical breast examination on breast cancer incidence and mortality after 20 years: prospective, cluster randomised controlled trial in Mumbai[J]. BMJ, 2021, 372:n256. DOI:10.1136/bmj.n738.

- [6] Xia CF, Li H, Xu YJ, et al. Effect of an endoscopy screening on upper gastrointestinal cancer mortality: a community-based multicenter cluster randomized clinical trial[J]. *Gastroenterology*, 2025, 168(4): 725-740. DOI: 10.1053/j.gastro.2024.11.025.
- [7] Heitzer E, Haque IS, Roberts CES, et al. Current and future perspectives of liquid biopsies in genomics-driven oncology[J]. *Nat Rev Genet*, 2019, 20(2): 71-88. DOI: 10.1038/s41576-018-0071-5.
- [8] Duffy MJ. Carcinoembryonic antigen as a marker for colorectal cancer: is it clinically useful? [J] *Clin Chem*, 2001, 47(4):624-630.
- [9] Sturgeon CM, Duffy MJ, Stenman UH, et al. National academy of clinical biochemistry laboratory medicine practice guidelines for use of tumor markers in testicular, prostate, colorectal, breast, and ovarian cancers[J]. *Clin Chem*, 2008, 54(12):e11-79. DOI:10.1373/clinchem.2008.105601.
- [10] Sawyers CL. The cancer biomarker problem[J]. *Nature*, 2008, 452(7187):548-552. DOI:10.1038/nature06913.
- [11] Cohen JD, Li L, Wang YX, et al. Detection and localization of surgically resectable cancers with a multi-analyte blood test[J]. *Science*, 2018, 359(6378):926-930. DOI: 10.1126/science.aar3247.
- [12] Lennon AM, Buchanan AH, Kinde I, et al. Feasibility of blood testing combined with PET-CT to screen for cancer and guide intervention[J]. *Science*, 2020, 369(6499): eabb9601. DOI:10.1126/science.abb9601.
- [13] Cristiano S, Leal A, Phallen J, et al. Genome-wide cell-free DNA fragmentation in patients with cancer[J]. *Nature*, 2019, 570(7761): 385-389. DOI: 10.1038/s41586-019-1272-6.
- [14] Liu MC, Oxnard GR, Klein EA, et al. Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA[J]. *Ann Oncol*, 2020, 31(6): 745-759. DOI:10.1016/j.annonc.2020.02.011.
- [15] Klein EA, Richards D, Cohn A, et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set[J]. *Ann Oncol*, 2021, 32(9):1167-1177. DOI:10.1016/j.annonc.2021.05.806.
- [16] Schrag D, Beer TM, McDonnell 3rd CH, et al. Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study[J]. *Lancet*, 2023, 402(10409): 1251-1260. DOI:10.1016/S0140-6736(23)01700-2.
- [17] Charles S, Richard DN, Peter WMJ, et al. NHS-Galleri trial design: equitable study recruitment tactics for targeted population-level screening with a multi-cancer early detection (MCED) test[J]. *JCO*, 2022, 40: TPS6606. DOI: 10.1200/JCO.2022.40.16_suppl.TPS6606.
- [18] Kandimalla R, Xu JF, Link A, et al. EpiPanGI Dx: a cell-free DNA methylation fingerprint for the early detection of gastrointestinal cancers[J]. *Clin Cancer Res*, 2021, 27(22): 6135-6144. DOI:10.1158/1078-0432.CCR-21-1982.
- [19] Gao Q, Lin YP, Li BS, et al. Unintrusive multi-cancer detection by circulating cell-free DNA methylation sequencing (THUNDER): development and independent validation studies[J]. *Ann Oncol*, 2023, 34(5): 486-495. DOI:10.1016/j.annonc.2023.02.010.
- [20] Ding Z, Song L, Jiang Z, et al. 97P GENIE-seq: A novel methylation sequencing method for effective and accurate identification of methylation markers from cfDNA[J]. *Annals of Oncology*, 2024, 35(2):S253. DOI: 10.1016/j.annonc.2024.08.105.
- [21] He XS, Ma SH, Xu H, et al. Development and clinical validation of a cell-free DNA methylation sequencing test for multi-cancer early detection[J]. *J Clin Oncol*, 2025, 43: 10537. DOI:10.1200/JCO.2025.43.16_suppl.10537.
- [22] Chen XD, Gole J, Gore A, et al. Non-invasive early detection of cancer four years before conventional diagnosis using a blood test[J]. *Nat Commun*, 2020, 11(1): 3475. DOI: 10.1038/s41467-020-17316-z.
- [23] Bao H, Chen XX, Wu M, et al. Abstract 1266: development and performance of a multi-cancer early detection test utilizing plasma cfDNA fragmentomics: a large-scale, prospective, multicenter study[J]. *Cancer Res*, 2024, 84(Suppl 6):1266. DOI:10.1158/1538-7445.AM2024-1266.
- [24] Lo YMD, Han DSC, Jiang PY, et al. Epigenetics, fragmentomics, and topology of cell-free DNA in liquid biopsies[J]. *Science*, 2021, 372(6538):eaaw3616. DOI: 10.1126/science.aaw3616.
- [25] Lapitz A, Azkargorta M, Milkiewicz P, et al. Liquid biopsy-based protein biomarkers for risk prediction, early diagnosis, and prognostication of cholangiocarcinoma[J]. *J Hepatol*, 2023, 79(1): 93-108. DOI: 10.1016/j.jhep.2023.02.027.
- [26] Giuliano M, Giordano A, Jackson S, et al. Circulating tumor cells as early predictors of metastatic spread in breast cancer patients with limited metastatic dissemination[J]. *Breast Cancer Res*, 2014, 16(5): 440. DOI: 10.1186/s13058-014-0440-8.
- [27] Xu ZZ, Ge GZ, Guan B, et al. Noninvasive detection and localization of genitourinary cancers using urinary sediment DNA methylomes and copy number profiles[J]. *Eur Urol*, 2020, 77(2): 288-290. DOI: 10.1016/j.eururo.2019.11.006.
- [28] Snoek BC, Splunter APV, Bleeker MCG, et al. Cervical cancer detection by DNA methylation analysis in urine[J]. *Sci Rep*, 2019, 9(1):3088. DOI:10.1038/s41598-019-39275-2.
- [29] Helder RVD, Steenbergen RDM, Splunter APV, et al. HPV and DNA methylation testing in urine for cervical intraepithelial neoplasia and cervical cancer detection[J]. *Clin Cancer Res*, 2022, 28(10):2061-2068. DOI:10.1158/1078-0432.CCR-21-3710.
- [30] Óscar IV, Rosa MLP, Jose GSerrano, et al. Salivary LDH in oral cancer and potentially malignant disorders: a systematic review and meta-analysis[J]. *Oral Dis*, 2022, 28(1):44-56. DOI:10.1111/odi.13630.
- [31] Cabezas CS, Pérez AR, García BV, et al. ctDNA detection in cerebrospinal fluid and plasma and mutational concordance with the primary tumor in a multicenter prospective study of patients with glioma[J]. *Ann Oncol*, 2025, 36(6):660-672. DOI:10.1016/j.annonc.2025.02.005.
- [32] Xing SZ, Zhu YM, You YX, et al. Cell-free RNA for the liquid biopsy of gastrointestinal cancer[J]. *Wiley Interdiscip Rev RNA*, 2023, 14(5):e1791. DOI:10.1002/wrna.1791.
- [33] Wang J, Huang JY, Hu YL, et al. Terminal modifications independent cell-free RNA sequencing enables sensitive early cancer detection and classification[J]. *Nat Commun*, 2024, 15(1):156. DOI:10.1038/s41467-023-44461-y.
- [34] Montgomery A, Tsiatsianis GC, Mouratidis I, et al. Utilizing nullomers in cell-free RNA for early cancer detection[J]. *Cancer Gene Ther*, 2024, 31(6): 861-870. DOI: 10.1038/

- s41417-024-00741-3.
- [35] In 't Veld SGJG, Arkani M, Post E, et al. Detection and localization of early- and late-stage cancers using platelet RNA[J]. *Cancer Cell*, 2022, 40(9): 999-1009. e6. DOI: 10.1016/j.ccell.2022.08.006.
 - [36] Liu ZZ, Wang TF, Yang X, et al. Polyadenylation ligation-mediated sequencing (PALM-Seq) characterizes cell-free coding and non-coding RNAs in human biofluids [J]. *Clin Transl Med*, 2022, 12(7): e987. DOI: 10.1002/ctm2.987.
 - [37] Mahmodul HS. Extracellular/circulating microRNAs: release mechanisms, functions and challenges[J]. *Achievements in the Life Sciences*, 2016, 10(2): 175-186. DOI:10.1016/j.als.2016.11.007.
 - [38] So JBY, Kapoor R, Zhu F, et al. Development and validation of a serum microRNA biomarker panel for detecting gastric cancer in a high-risk population[J]. *Gut*, 2021, 70(5):829-837. DOI:10.1136/gutjnl-2020-322065.
 - [39] Ying LS, Du LB, Zou RY, et al. Development of a serum miRNA panel for detection of early stage non-small cell lung cancer[J]. *Proc Natl Acad Sci U S A*, 2020, 117(40): 25036-25042. DOI:10.1073/pnas.2006212117.
 - [40] Zou RY, Loke SY, Tan VKM, et al. Development of a microRNA panel for classification of abnormal mammograms for breast cancer[J]. *Cancers (Basel)*, 2021, 13(9):2130. DOI:10.3390/cancers13092130.
 - [41] Luan Y, Zhong GL, Li SY, et al. A panel of seven protein tumour markers for effective and affordable multi-cancer early detection by artificial intelligence: a large-scale and multicentre case-control study[J]. *EClinicalMedicine*, 2023, 61:102041. DOI:10.1016/j.eclinm.2023.102041.
 - [42] Polasky DA, Yu FC, Teo GC, et al. Fast and comprehensive N- and O-glycoproteomics analysis with MSFragger-Glyco [J]. *Nat Methods*, 2020, 17(11):1125-1132. DOI:10.1038/s41592-020-0967-9.
 - [43] Papier K, Atkins JR, Tong TYN, et al. Identifying proteomic risk factors for cancer using prospective and exome analyses of 1463 circulating proteins and risk of 19 cancers in the UK Biobank[J]. *Nat Commun*, 2024, 15(1): 4010. DOI:10.1038/s41467-024-48017-6.
 - [44] Taylor MS, Wu C, Fridy PC, et al. Ultrasensitive detection of circulating LINE-1 ORF1p as a specific multicancer biomarker[J]. *Cancer Discov*, 2023, 13(12): 2532-2547. DOI:10.1158/2159-8290.CD-24-0862.
 - [45] Wishart DS. Is cancer a genetic disease or a metabolic disease? [J]. *EbioMedicine*, 2015, 2(6): 478-479. DOI: 10.1016/j.ebiom.2015.05.022.
 - [46] Yan L, Xu XP, Zeng CY, et al. Abstract LB255: MCTarg: a plasma-based metabolic biomarker model for multi-cancer early detection[J]. *Cancer Res*, 2025, 85(8 Suppl 2): LB225. DOI:10.1158/1538-7445.AM2025-LB255.
 - [47] Zhang H, Zhao L, Jiang JJ, et al. Multiplexed nanomaterial-assisted laser desorption/ionization for pan-cancer diagnosis and classification[J]. *Nat Commun*, 2022, 13(1):617. DOI:10.1038/s41467-021-26642-9.
 - [48] Kim SY, Jeong S, Lee W, et al. Cancer signature ensemble integrating cfDNA methylation, copy number, and fragmentation facilitates multi-cancer early detection[J]. *Exp Mol Med*, 2023, 55(11): 2445-2460. DOI: 10.1038/s12276-023-01119-5.
 - [49] Lin ZA, Chip Stewart, Elizabeth EM. et al. Abstract 5162: TuFEst: a sensitive and cost-effective pan-cancer detection approach with accurate tumor fraction estimation[J]. *Cancer Res*, 2022, 82(Suppl 12):5162. DOI:10.1158/1538-7445.AM2022-5162.
 - [50] Ju J, Zhao X, An YY, et al. Cell-free DNA end characteristics enable accurate and sensitive cancer diagnosis[J]. *Cell Rep Methods*, 2024, 4(10):100877. DOI:10.1016/j.crmeth.2024.100877.
 - [51] Xie L, Du XD, Wang SN, et al. Development and evaluation of cancer differentiation analysis technology: a novel biophysics-based cancer screening method[J]. *Expert Rev Mol Diagn*, 2022, 22(1):111-117. DOI:10.1080/14737159.2021.2013201.
 - [52] Yu CC, Du XD, Lin Y, et al. Significant results from a major multi-year, multi-cancer follow-up study with an enrollment of over 19,000 individuals[J]. *J Clin Oncol*, 2024, 42(Suppl 16):10539. DOI:10.1200/JCO.2024.42.16_suppl.10539.
 - [53] Nguyen LHD, Nguyen THH, Le VH, et al. Prospective validation study: a non-invasive circulating tumor DNA-based assay for simultaneous early detection of multiple cancers in asymptomatic adults[J]. *BMC Med*, 2025, 23(1):90. DOI:10.1186/s12916-025-03929-y.
 - [54] Vaisvila R, Ponnaluri VKC, Sun ZY, et al. Enzymatic methyl sequencing detects DNA methylation at single-base resolution from picograms of DNA[J]. *Genome Res*, 2021, 31(7):1280-1289. DOI:10.1101/gr.266551.120.
 - [55] Olova N, Krueger F, Andrews S, et al. Comparison of whole-genome bisulfite sequencing library preparation strategies identifies sources of biases affecting DNA methylation data[J]. *Genome Biol*, 2018, 19(1): 33. DOI: 10.1186/s13059-019-1656-9.
 - [56] Weber M, Davies JJ, Wittig D, et al. Chromosome-wide and promoter-specific analyses identify sites of differential DNA methylation in normal and transformed human cells [J]. *Nat Genet*, 2005, 37(8):853-862. DOI:10.1038/ng1598.
 - [57] Melnikov AA, Gartenhaus RB, Levenson AS, et al. MSRE-PCR for analysis of gene-specific DNA methylation [J]. *Nucleic Acids Res*, 2005, 33(10): e93. DOI: 10.1093/nar/gni092.
 - [58] Morrison J, Koeman JM, Johnson BK, et al. Evaluation of whole-genome DNA methylation sequencing library preparation protocols[J]. *Epigenetics Chromatin*, 2021, 14(1):28. DOI:10.1186/s13072-021-00401-y.
 - [59] Deveson IW, Gong BS, Lai K, et al. Evaluating the analytical validity of circulating tumor DNA sequencing assays for precision oncology[J]. *Nat Biotechnol*, 2021, 39(9): 1115-1128. DOI:10.1038/s41587-021-00857-z.
 - [60] Deng ZZ, Ji YK, Han B, et al. Early detection of hepatocellular carcinoma via no end-repair enzymatic methylation sequencing of cell-free DNA and pre-trained neural network[J]. *Genome Med*, 2023, 15(1): 93. DOI: 10.1186/s13073-023-01238-8.
 - [61] Zhou L, Ng HK, Drautz MDI, et al. Systematic evaluation of library preparation methods and sequencing platforms for high-throughput whole genome bisulfite sequencing [J]. *Sci Rep*, 2019, 9(1): 10383. DOI: 10.1038/s41598-019-46875-5.
 - [62] Bie FL, Wang ZJ, Li YL, et al. Multimodal analysis of cell-free DNA whole-methylome sequencing for cancer detection and localization[J]. *Nat Commun*, 2023, 14(1):

6042. DOI:10.1038/s41467-023-41774-w.
- [63] 国家药品监督管理局. 人工智能医用软件产品分类界定指导原则 [EB/OL]. (2021-07-08) [2025-06-25]. https://www.beijing.gov.cn/zhengce/zhengcefaui/qtwj/202204/t20220408_2669468.html.
- [64] 国家卫生健康委. 健康中国行动—癌症防治行动实施方案(2023—2030 年) [EB/OL]. (2023-10-30) [2025-06-25]. https://www.gov.cn/zhengce/zhengceku/202311/content_6915380.htm.
- [65] 国家药监局器审中心. 国家药监局器审中心关于发布人工智能医疗器械注册审查指导原则的通告(2022 年第 8 号) [EB/OL]. (2022-03-14) [2025-06-25]. <https://www.ccfde.org/zryyxxw/cfdazsjg/ylqxjs/webinfo/2022/03/1648289422620244.htm>.
- [66] 国家药品监督管理局. 人工智能医疗器械 质量要求和评价 第 3 部分: 数据标注通用要求 [EB/OL]. (2022-08-17) [2025-06-25]. <https://www.cmde.org.cn/hbpdf/YY1833.3-2022.pdf>.
- [67] 国家药品监督管理局. 人工智能医疗器械 质量要求和评价 第 2 部分: 数据集通用要求 [EB/OL]. (2022-07-01) [2025-06-25]. <https://www.cmde.org.cn/hbpdf/YY1833.2-2022.pdf?type=pc&m=>.
- [68] 国家药品监督管理局医疗器械技术审评中心. 关于公开征求《肿瘤筛查用体外诊断试剂临床评价注册审查指导原则(征求意见稿)》等 2 项指导原则意见的通知 [EB/OL]. (2024-01-19) [2025-06-25]. <https://www.cmde.org.cn/zhuanti/zqyj/20240122110450158.html>.
- [69] Clarke CA, Hubbell E, Kurian AW, et al. Projected reductions in absolute cancer-related deaths from diagnosing cancers before metastasis, 2006-2015[J]. *Cancer Epidemiol Biomarkers Prev*, 2020, 29(5):895-902. DOI:10.1158/1055-9965.EPI-19-1366.
- [70] Hubbell E, Clarke CA, Aravanis AM, et al. Modeled reductions in late-stage cancer with a multi-cancer early detection test[J]. *Cancer Epidemiol Biomarkers Prev*, 2021, 30(3):460-468. DOI:10.1158/1055-9965.EPI-20-1134.
- [71] Mizrahi JD, Surana R, Valle JW, et al. Pancreatic cancer[J]. *Lancet*, 2020, 395(10242): 2008-2020. DOI: 10.1016/S0140-6736(20)30974-0.
- [72] 王婷, 秦毅, 徐晓武, 等. 2024 年胰腺癌研究及诊疗新进展[J]. *中国癌症杂志*, 2025, 35(1): 1-11. DOI: 10.19401/j.cnki.1007-3639.2025.01.001.
- [73] Buys SS, Partridge E, Black A, et al. Effect of screening on ovarian cancer mortality: the prostate, lung, colorectal and ovarian (PLCO) cancer screening randomized controlled trial[J]. *JAMA*, 2011, 305(22): 2295-303. DOI: 10.1001/jama.2011.766.
- [74] Pinsky PF, Yu K, Kramer BS, et al. Extended mortality results for ovarian cancer screening in the PLCO trial with median 15years follow-up[J]. *Gynecol Oncol*, 2016, 143(2):270-275. DOI:10.1016/j.ygyno.2016.08.334.
- [75] Menon U, Maharaj AG, Burnell M, et al. Ovarian cancer population screening and mortality after long-term follow-up in the UK collaborative trial of ovarian cancer screening (UKCTOCS): a randomised controlled trial[J]. *Lancet*, 2021, 397(10290): 2182-2193. DOI: 10.1016/S0140-6736(21)00731-5.
- [76] 中国老年保健协会妇科肿瘤专业委员会, 中国医师协会妇产科医师分会, 沈杨. 卵巢癌早期筛查中国专家共识(2025 年版)[J]. *中国实用妇科与产科杂志*, 2025, 41(2): 204-211. DOI:10.19538/j.fk2025020113.
- [77] 中华医学会消化内镜学分会胰腺疾病协作组. 中国胰腺癌高危人群早期筛查和监测共识意见(2021,南京)[J]. *临床肝胆病杂志*, 2022, 38(5):1016-1022. DOI: 10.3969/j.issn.1001-5256.2022.05.008.
- [78] Flowers CR, Sinha R, Vose JM. Improving outcomes for patients with diffuse large B-cell lymphoma[J]. *CA Cancer J Clin*, 2010, 60(6):393-408. DOI:10.3322/caac.20087.
- [79] Wang YD, Jia SZ, Cao XB, et al. Application of next-generation sequencing in diffuse large B-cell lymphoma[J]. *Pharmacogenomics*, 2023, 24(1): 59-68. DOI:10.2217/pgs-2022-0140.
- [80] Liu J, Song B, Fan TY, et al. Pathological and clinical characteristics of 1,248 non-Hodgkin's lymphomas from a regional cancer hospital in Shandong, China[J]. *Asian Pac J Cancer Prev*, 2011, 12(11):3055-3061.
- [81] Poppel HV, Albrecht T, Basu P, et al. Serum PSA-based early detection of prostate cancer in Europe and globally: past, present and future[J]. *Nat Rev Urol*, 2022, 19(9):562-572. DOI:10.1038/s41585-022-00638-6.
- [82] Liu JZ, Dong L, Zhu YJ, et al. Prostate cancer treatment - China's perspective[J]. *Cancer Lett*, 2022, 550: 215927. DOI:10.1016/j.canlet.2022.215927.
- [83] Wang YX, Springer S, Zhang M, et al. Detection of tumor-derived DNA in cerebrospinal fluid of patients with primary tumors of the brain and spinal cord[J]. *Proc Natl Acad Sci U S A*, 2015, 112(31):9704-9709. DOI: 10.1073/pnas.1511694112.
- [84] Bale TA, Yang SR, Solomon JP, et al. Clinical experience of cerebrospinal fluid-based liquid biopsy demonstrates superiority of cell-free DNA over cell pellet genomic DNA for molecular profiling[J]. *J Mol Diagn*, 2021, 23(6): 742-752. DOI:10.1016/j.jmoldx.2021.03.001.
- [85] Kisiel JB, Papadopoulos N, Liu MC, et al. Multicancer early detection test: preclinical, translational, and clinical evidence-generation plan and provocative questions[J]. *Cancer*, 2022, 128(4):861-874. DOI:10.1002/cnrc.33912.
- [86] Jamshidi A, Liu MC, Klein EA, et al. Evaluation of cell-free DNA approaches for multi-cancer early detection[J]. *Cancer Cell*, 2022, 40(12):1537-1549.e12. DOI:10.1016/j.ccell.2022.10.022.
- [87] Moran B, Das S, Smeets D, et al. Assessment of concordance between fresh-frozen and formalin-fixed paraffin embedded tumor DNA methylation using a targeted sequencing approach[J]. *Oncotarget*, 2017, 8(29):48126-48137. DOI:10.18632/oncotarget.18296.
- [88] Imai M, Nakamura Y, Yoshino T. Transforming cancer screening: the potential of multi-cancer early detection (MCED) technologies[J]. *Int J Clin Oncol*, 2025, 30(2): 180-193. DOI:10.1007/s10147-025-02694-5.
- [89] Glenn DB, Joshua JO. Criteria for evaluating multi-cancer early detection tests[J]. *Oncology & Haematology*, 2021, 17(1):3-6. DOI:<https://doi.org/10.17925/OHR.2021.17.1.3>.
- [90] Iwagami M, Shinozaki T. Introduction to matching in case-control and cohort studies[J]. *Ann Clin Epidemiol*, 2022, 4(2):33-40. DOI:10.37737/ace.22005.
- [91] Dongen JV, Nivard MG, Willemsen G, et al. Genetic and environmental influences interact with age and sex in shaping the human methylome[J]. *Nat Commun*, 2016, 7: 11115. DOI:10.1038/ncomms11115.
- [92] Nadauld L, McDonnell 3rd CH, Dilaveri CA, et al. Psychosocial impact associated with a multicancer early

- detection test (PATHFINDER): a prospective, multicentre, cohort study[J]. *Lancet Oncol*, 2025, 26(2):165-174. DOI: 10.1016/S1470-2045(24)00645-4.
- [93] Kerlikowske K, Grady D, Rubin SM, et al. Efficacy of screening mammography. A meta-analysis[J]. *JAMA*, 1995, 273(2):149-154.
- [94] Quintero E, Castells A, Bujanda L, et al. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening[J]. *N Engl J Med*, 2012, 366(8): 697-706. DOI: 10.1056/NEJMx150040.
- [95] Forsberg A, Westerberg M, Metcalfe C, et al. Once-only colonoscopy or two rounds of faecal immunochemical testing 2 years apart for colorectal cancer screening (SCREESCO): preliminary report of a randomised controlled trial[J]. *Lancet Gastroenterol Hepatol*, 2022, 7(6):513-521. DOI:10.1016/S2468-1253(21)00473-8.
- [96] Carr D, Kent DM, Welch HG. All-cause mortality as the primary endpoint for the GRAIL/National Health Service England multi-cancer screening trial[J]. *J Med Screen*, 2022, 29(1):3-6. DOI:10.1177/09691413211059638.
- [97] Duffy SW. All-cause mortality in multi-cancer screening trials[J]. *J Med Screen*, 2022, 29(1): 1-2. DOI: 10.1177/09691413211060680.
- [98] Webb AB, Berg CD, Castle PE, et al. Considerations for using potential surrogate endpoints in cancer screening trials[J]. *Lancet Oncol*, 2024, 25(5): e183-e192. DOI: 10.1016/S1470-2045(24)00015-9.
- [99] Klein EA, Madhavan S, Beer TM, et al. Dying to find out: the cost of time at the dawn of the multicancer early detection era[J]. *Cancer Epidemiol Biomarkers Prev*, 2023, 32(8):1003-1010. DOI:10.1158/1055-9965.EPI-22-1275.
- [100] Friends of cancer research. Multi-cancer early detection screening tests: considerations for use of real-world data [EB/OL]. [2025-06-25]. https://friendsofcancerresearch.org/wp-content/uploads/MCED_Screening_Tests-Considerations_for_Use_of_Real-World_Data.pdf.
- [101] Feng XS, Zahed H, Onwuka J, et al. Cancer stage compared with mortality as end points in randomized clinical trials of cancer screening: a systematic review and meta-analysis [J]. *JAMA*, 2024, 331(22): 1910-1917. DOI:10.1001/jama.2024.5814.
- [102] Clarke CA, Lang K, Putcha G, et al. BLOODPAC: Collaborating to chart a path towards blood-based screening for early cancer detection[J]. *Clin Transl Sci*, 2023, 16(1):5-9. DOI:10.1111/cts.13427.
- [103] Owens L, Gulati R, Etzioni R. Stage shift as an endpoint in cancer screening trials: implications for evaluating multicancer early detection tests[J]. *Cancer Epidemiol Biomarkers Prev*, 2022, 31(7):1298-1304. DOI:10.1158/1055-9965.EPI-22-0024.
- [104] Hu P, Prorok PC, Katki HA. Design of randomized controlled trials to estimate cancer-mortality reductions from multicancer detection screening[J]. *J Natl Cancer Inst*, 2025, 117(2):303-311. DOI:10.1093/jnci/djae247.
- [105] Kerlikowske K, Bissell MCS, Sprague BL, et al. Advanced breast cancer definitions by staging system examined in the breast cancer surveillance consortium[J]. *J Natl Cancer Inst*, 2021, 113(7): 909-916. DOI: 10.1093/jnci/djaa176.
- [106] Singal AG, Parikh ND, Kanwal F, et al. National liver cancer screening trial (TRACER) study protocol[J]. *Hepatol Commun*. 2024, 8(11):e0565. DOI:10.1097/HC9.0000000000000565.
- [107] Dai JY, Luebeck EG, Chang ET, et al. Strong association between reduction of late-stage cancers and reduction of cancer-specific mortality in meta-regression of randomized screening trials across multiple cancer types[J]. *J Med Screen*, 2024, 31(4):211-222. DOI:10.1177/09691413241256744.
- [108] 国家癌症中心. 2020 中国肿瘤登记年报[M]. 北京: 人民卫生出版社, 2020.
- [109] Hoffman RM, Wolf AMD, Raoof S, et al. Multicancer early detection testing: Guidance for primary care discussions with patients[J]. *Cancer*, 2025, 131(7): e35823. DOI: 10.1002/cncr.35823.
- [110] Li T, Mello TC, Brennan PC. Descriptive epidemiology of breast cancer in China: incidence, mortality, survival and prevalence[J]. *Breast Cancer Res Treat*, 2016, 159(3): 395-406. DOI:10.1007/s10549-016-3947-0.
- [111] Chan KH, Wright N, Xiao D, et al. Tobacco smoking and risks of more than 470 diseases in China: a prospective cohort study[J]. *Lancet Public Health*, 2022, 7(12): e1014-e1026. DOI:10.1016/S2468-2667(22)00227-4.
- [112] GBD 2015 Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990-2015: a systematic analysis from the Global Burden of Disease Study 2015[J]. *Lancet*, 2017, 389(10082): 1885-1906. DOI: 10.1016/S0140-6736(17)30819-X.
- [113] IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Alcohol drinking[M]. Lyon: IARC Monogr Eval Carcinog Risks Hum, 1988, 44:1-378.
- [114] Secretan BL, Scoccianti C, Loomis D, et al. Body fatness and cancer--viewpoint of the IARC working group[J]. *N Engl J Med*, 2016, 375(8):794-798. DOI:10.1056/NEJMSr1606602.
- [115] Tsilidis KK, Kasimis JC, Lopez DS, et al. Type 2 diabetes and cancer: umbrella review of meta-analyses of observational studies[J]. *BMJ*, 2015, 350:g7607. DOI: 10.1136/bmj.g7607.
- [116] Durham DD, Abraham LA, Roberts MC, et al. Breast cancer incidence among women with a family history of breast cancer by relative's age at diagnosis[J]. *Cancer*, 2022, 128(24):4232-4240. DOI:10.1002/cncr.34365.
- [117] Brune KA, Lau B, Palmisano E, et al. Importance of age of onset in pancreatic cancer kindreds[J]. *J Natl Cancer Inst*, 2010, 102(2):119-126. DOI:10.1093/jnci/djp466.
- [118] Sun DQ, Li H, Cao MM, et al. Cancer burden in China: trends, risk factors and prevention[J]. *Cancer Biol Med*, 2020, 17(4): 879-895. DOI: 10.20892/j. issn. 2095-3941. 2020.0387.
- [119] FDA. November 29, 2023: Molecular and clinical genetics panel of the medical devices advisory committee meeting announcement[EB/OL]. [2025-06-25]. <https://www.fda.gov/advisory-committees/advisory-committee-calendar/november-29-2023-molecular-and-clinical-genetics-panel-medical-devices-advisory-committee-meeting>.