

文章编号: 1000-2812 (2023) 11-0072-08

《中国男性乳腺癌临床诊治实践指南(2023版)》 诊疗解读

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摘要: 男性乳腺癌发病罕见, 预后较差, 以往只能参考女性乳腺癌相关指南进行诊疗。中华医学会外科学分会乳腺外科学组共同制定的《中国男性乳腺癌临床诊治实践指南(2023版)》于2023年2月4日首次发布, 该指南结合中国国情对男性乳腺癌管理的各个环节进行了详细阐述并作出相应推荐, 是国内首部男性乳腺癌诊疗指南。本文通过查阅相关文献, 对该指南中男性乳腺癌的诊疗内容进行详细解读。

关键词: 男性乳腺癌; 诊断; 治疗; 指南; 解读

中图分类号: R737.9 文献标识码: A doi: 10.13885/j.issn.1000-2812.2023.11.011

Interpretation of *Clinical practice China guidelines for male breast cancer* (2023 edition)

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Abstract: Male breast cancer is rare and has a poor prognosis. Prospective data in the management of male breast cancer are lacking, and the majority of treatment strategies are adopted from the established guidelines for female breast cancer. The *Clinical Practice China Guidelines for Male Breast Cancer* (2023 edition) jointly formulated by the Chinese Society of Breast Surgery, Chinese Society of Surgery and Chinese Medical Association was first published on February 4, 2023. The guidelines elaborate and make recommendations on various aspects of male breast cancer management in accordance with the Chinese national status. This article aimed at making a detailed interpretation of the diagnosis and treatment contents of male breast cancer in the guidelines by referring to relevant literature.

Keywords: male breast cancer; diagnosis; guideline; therapy; interpretation

男性乳腺癌是一种特殊类型的乳腺恶性肿瘤, 约占所有乳腺癌的1%, 其发病罕见、恶性程度较高, 预后较差, 死亡率高于女性乳腺癌^[1]。此前国内缺乏关于男性乳腺癌患者临床管理的相关指南, 其诊治多需参照女性乳腺癌指南进行。《中国

男性乳腺癌临床诊治实践指南(2023版)》(简称2023男乳指南)于2023年2月4日发表, 是中华医学会外科学分会乳腺外科学组共同制定的中国首部关于男性乳腺癌的诊疗指南, 旨在提高中国男性乳腺癌诊疗流程的规范性和科学性^[2]。本文主要

收稿日期: 2023-09-08

基金项目: 北京健康促进会“中国乳腺外科青年医师研究”奖励基金资助项目(2020-CHPASLP); 兰州大学第二医院“萃英学子科研培育”计划资助项目(CYXZ2021-40)

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对 2023 男乳指南诊疗相关内容进行详细解读。

1 诊断

2023 男乳指南推荐男性乳腺癌的诊断需要结合患者的临床表现、体格检查、影像学和组织病理学检查等,并对临床表现及诊断方法两项内容作出了详细推荐,此外还提及男性乳腺癌患者 BRCA 基因突变风险及基因检测的相关内容。

1.1 临床表现

2023 男乳指南指出乳房肿块与腋窝淋巴结肿大是男性乳腺癌的主要临床表现^[2]。Accomasso 等^[3]研究显示 73.5% 的男性乳腺癌患者首发症状为乳房肿块,26.5% 的患者因发现乳头改变而就诊。欧洲癌症研究与治疗组织的研究结果显示接近 40% 的男性乳腺癌患者有腋窝淋巴结转移^[4],Yadav 等^[5]报告美国男性乳腺癌患者淋巴结阳性率约为 36%,Xi 等^[6]报告的东亚男性乳腺癌患者腋窝淋巴结阳性比例为 30.2%。除乳房肿物与腋窝淋巴结肿大外,男性乳腺癌临床表现还可有血性乳头溢液、乳头回缩、皮肤或胸肌粘连、Paget 病等表现^[7-9]。但上述临床表现并不多见,其发生率鲜有文献提供可靠数据。此外也有文献报道男性乳腺癌还可表现为界限清晰的囊性肿物^[10]、隐匿性乳腺癌^[11]等罕见表现。

1.2 影像学检查

在影像学检查方面,2023 男乳指南推荐了超声检查与 X 线检查。超声检查具有方便、无创、低成本、无辐射等优势,Rong 等^[12]的研究结果显示超声检查检测男性乳腺恶性肿瘤的敏感性、特异性、阳性预测值(positive predictive value, PPV)、阴性预测值(negative predictive value, NPV)和准确性分别为 100%、99.3%、69.2%、100% 和 97.7%。2023 男乳指南提到超声检查在肿物定位及其与乳头关系中具有较高价值,并且在评价腋窝淋巴结受累方面表现良好,对超声检查作出 IA 类推荐。对于乳房 X 线检查,Gao 等^[13]的研究显示在人群筛查中,乳房 X 线检查对男性乳腺癌的敏感性、特异性、PPV 和 NPV 分别为 100%、95%、50% 和 100%;在诊断中乳房 X 线检查的敏感性、特异性、PPV 和 NPV 分别为 94.7%、92.4%、25.9% 和 99.9%。Healy 等^[14]的结果则显示乳腺 X

线检查的敏感性、特异性、PPV、NPV 分别为 84.6%、99.4%、69.8% 和 99.8%。但男性乳房体积小,X 线检查可能会存在技术上的困难。此外,男性胸大肌较为发达,可能会掩盖可疑病变。在诊断方面,2023 男乳指南对男性乳房磁共振成像(magnetic resonance imaging, MRI)未作出推荐,指出 MRI 对男性乳腺疾病诊断价值有限,多用于评估胸壁受累、术后残留病灶、新辅助化疗反应等^[2]。目前,文献中很少提到 MRI 在男性乳腺癌诊断中的作用,仅个别报道显示在常规检查及穿刺活检结果模棱两可但临床高度怀疑时,MRI 可协助诊断、排除隐匿性恶性肿瘤及发现对侧病灶^[15-17]。此外,近年也有正电子发射断层显像在男性乳房检查中的应用个例^[18],提示对于特定个体,指南推荐以外的其他检查方式也可谨慎斟酌使用,明确诊断。强调不同检查手段的结合,利用各自优势,作出最终诊断。

1.3 组织病理学检查

组织病理检查为男性乳腺癌诊断的金标准,活检一般有以下几种方法:开放手术活检、细针抽吸活检(fine-needle aspiration biopsy, FNAB)、空芯针穿刺活检(core needle biopsy, CNB)、真空辅助乳腺活检(vacuum-assisted breast biopsy, VABB)。目前临床实践中乳腺肿物活检以 CNB 为主,因为它更能明确诊断浸润性乳腺癌。此外研究显示乳腺疾病的 VABB 较 CNB 有更高的敏感性 & 更低的漏诊率和低估率^[19],但其在男性乳腺癌方面并没有足够的证据支持。2023 男乳指南推荐了 CNB 作为男性乳腺癌乳腺组织活检方法,不推荐 FNAB。Hoda 等^[20]报道 FNAB 检测男性乳腺癌的敏感性为 95.8%,特异性为 100%。但 FNAB 获取的组织量较少并可能存在标本不合格等缺点。Yang 等^[21]评估了 CNB 在男性乳腺病变中的效用,结果显示 CNB 在男性中安全可行,可获取足够样本、能有效鉴别良恶性病变,CNB 的敏感性为 98.9%,特异性为 100%,PPV 为 100%,NPV 为 99.3%,总体准确率为 99.6%。近年随着 VABB 在女性乳腺癌中应用广泛,其在男性乳腺癌中也逐渐被采用,但指南指出 VABB 需要有经验的医生完成,主要考虑到男性乳腺腺体组织量不多,且病灶多位于乳晕下方^[22]。对于腋窝淋巴结的活检,

指南推荐了FNAB与CNB两种方式。Huang等^[23]研究了FNAB区分腋窝肿块恶性和良性病变的诊断能力,结果显示FNAB的敏感性为95.98%,特异性为99.56%,PPV为97.45%,NPV为99.29%,明确了FNAB在评估腋窝肿物中的效用。Fujioka等^[24]的研究结果显示,在腋窝肿物的评估中FNAB的敏感性为90.9%,特异性为90.0%,准确率为90.7%;CNB的敏感性为95.8%,特异性为100%,准确率为97.0%。超声引导下的FNAB和CNB在腋窝淋巴结肿大男性乳腺癌患者的诊断中发挥着重要作用。

1.4 基因检测

男性乳腺癌的危险因素包括多种遗传与环境因素,但迄今为止,唯一明确的男性乳腺癌危险因素是乳腺癌易感基因1/2(breast cancer susceptibility gene 1/2, *BRCA1/2*)基因突变^[25],在2023男乳指南中也提到*BRCA1/2*突变携带者的男性乳腺癌累积风险均高于非携带者^[2]。目前普遍认为*BRCA1/2*基因致病突变或可能致病突变的携带者患乳腺癌的风险明显提高^[26]。*BRCA1/2*基因突变在女性乳腺癌中与侵袭性高的分子表型、早期发病和乳腺癌家族史有关^[27],但在男性乳腺癌中并未发现类似结果^[28]。此外*BRCA1/2*基因突变与乳腺癌不良生存结局相关的证据不论是在女性乳腺癌还是男性乳腺癌中均存在争议^[29]。男性乳腺癌基因检测主要可指导癌症患者后续的个体化治疗,如多腺苷二磷酸核糖聚合酶抑制剂的选择。多项研究纳入男性乳腺癌患者,确定了奥拉帕尼和他洛唑帕尼在转移性*BRCA*相关乳腺癌中的疗效^[27]。Ⅲ期OlympiaA试验中也纳入了男性乳腺癌患者,证明奥拉帕尼在辅助治疗中可提高早期乳腺癌患者的生存率^[30]。除指导靶向药物选择外,基因检测还可为患者亲属提供遗传与癌症防治建议,改善癌症患者亲属的预后^[31]。随着癌症诊断后生存率的提高,第二原发性癌症的发病也并不罕见,Allen等^[32]发现男性乳腺癌患者再患结直肠癌、胰腺癌和甲状腺癌的风险增高,这一结果也影响了男性乳腺癌患者基因检测、随访管理决策的制定。男性乳腺癌基因检测目前在部分发达国家已经基本覆盖,但中国乳腺癌患者基因检测普及率不高,加之男性乳腺癌发病率低,尚未有国内数据报告

基因检测在男性乳腺癌诊疗中的效用,2023男乳指南也未作常规推荐,但指南讨论部分指出男性乳腺癌患者可考虑行*BRCA1/2*基因检测。此外研究显示,除*BRCA1/2*突变外,还有多种基因突变也可增加男性乳腺癌患病风险,如乳腺癌易感基因相关蛋白2、共济失调毛细血管扩张突变基因等,这些可能在男性乳腺癌中更为常见(4.8% vs 1.8%)^[33]。多基因检测及遗传咨询将有助于填补高风险男性乳腺癌患者识别与管理方面的不足,并为患者及其家属提供针对性的癌症风险管理和决策。

2 治疗

2023男乳指南在治疗方面的内容主要集中在早期/局部/可手术的男性乳腺癌,对于新辅助治疗、局部晚期及转移性疾病的治疗此版本指南未对相关方案作出推荐,目前仍主要依据女性乳腺癌相关指南。

2.1 新辅助化疗

新辅助化疗主要用于原发肿瘤直径较大、腋窝淋巴结转移、人类表皮生长因子受体-2(human epidermal growth factor receptor-2, HER-2)阳性、三阴性(雌激素受体、孕激素受体和HER-2均为阴性)、有保乳意愿但瘤体乳腺体积比值较大难以保乳的乳腺癌患者^[34]。目前临床使用新辅助化疗的证据主要来自基于女性乳腺癌的研究,新辅助化疗在男性乳腺癌中的应用和有效性研究较少。2023男乳指南中无新辅助化疗方案推荐但建议男性乳腺癌患者新辅助化疗可参照女性乳腺癌进行。Schiza等^[35]比较了瑞典487例男性与82401例女性Ⅰ-Ⅲ期乳腺癌患者的新辅助化疗利用率与病理完全缓解率,结果显示新辅助化疗总利用率男性为4.9%,女性为7.8%,差异无统计学意义($OR_{校正}=1.135$, 95% *CI*: [0.606, 2.128]);在应用新辅助化疗的24例男性乳腺癌患者与6463例女性乳腺癌患者中,病理完全缓解率分别为16.7%和21.2%,差异无统计学意义($OR_{校正}=1.141$, 95% *CI*: [0.141, 9.238])。而Cao等^[36]关于美国人群的研究结果也支持上述结果,新辅助化疗可以降低男性乳腺癌患者乳房和腋窝的分期,但新辅助化疗在腋窝淋巴结阳性的男性乳腺癌患者中利用率相对较低,手术的使用相对积极。这

些结果支持新辅助化疗利用率及有效性无明显性别差异。但Leone等^[37]发现接受新辅助化疗的男性乳腺癌患者病理完全缓解率比例低于女性乳腺癌患者,可能是由于男性乳腺癌与女性乳腺癌病理特征不同所致。目前暂无前瞻性试验评估新辅助化疗在男性乳腺癌中的疗效,也没有研究对新辅助化疗的疗效进行前瞻性两性比较。

2.2 手术治疗

2.2.1 乳腺手术

2023男乳指南指出对于男性乳腺癌患者若无新辅助治疗指征,应首选手术治疗。对于乳房手术方式推荐了乳房切除术。Leone等^[38]分析了SEER数据库中1988—2017年6 919例男性乳腺癌患者,发现乳房切除术的总使用率为81.6%。此版本指南未对保留乳房的乳腺癌切除术(简称保乳手术)作出推荐,而Giordano^[39]的研究指出保乳手术利用率虽不高,但在男性乳腺癌中的安全性近似于女性乳腺癌。目前研究显示,保乳手术相比乳房全切术,患者的中位总生存期(overall survival, OS)没有明显的差别,5年和10年OS率也没有显著差异^[40]。Sauder等^[41]也发现在男性乳腺癌中,接受保乳手术和乳房切除术的患者在无病生存期(disease-free survival, DFS)、疾病特异性生存期及OS方面没有显著差异,但患者保乳手术后放疗的依从性低,强调手术方案医患双方共同决策的重要性。此外,保乳手术多为早期男性乳腺癌患者的可选手术方案,但男性缺乏乳腺组织,早期肿瘤即可累及乳头—乳晕复合体,保乳手术的选择仍存在一定争议,期待更多基于国人的前瞻性数据论证。

2.2.2 腋窝手术

对于腋窝淋巴结的处理,2023男乳指南推荐腋窝淋巴结阴性病人行前哨淋巴结活检,阳性病人则行腋窝淋巴结清扫。前哨淋巴结活检目前被用作女性乳腺癌患者的常规治疗,而Shang等^[42]的研究显示在早期男性乳腺癌中前哨淋巴结活检与腋窝淋巴结清扫在改善患者DFS($P=0.180$)和OS($P=0.055$)方面没有统计学差异,肯定了前哨淋巴结活检在男性乳腺癌中的效用。Lin等^[40]的研究也显示在男性乳腺癌中前哨淋巴结活检同样有较高的识别率(97.4%)与较低的假阴性率

(7.4%)。但值得注意的是,对于1~2个前哨淋巴结阳性的T1或T2期的男性乳腺癌患者,仅前哨淋巴结活检可能是不够的,Chung等^[43]发现在此类患者群体中,与单独使用前哨淋巴结活检相比,采用腋窝淋巴结清扫的患者具有更高的生存率。未来仍需更多的研究结果来优化对男性乳腺癌患者的腋窝管理。

2.3 放疗

关于放疗的选择,指南推荐Ⅲ期男性乳腺癌与淋巴结阳性男性乳腺癌患者行乳房切除术后接受辅助放疗。研究^[40]显示,与未接受放疗相比,乳房切除术后胸壁放疗显著改善OS($HR=0.67$, 95% CI: [0.54, 0.84]),乳房切除术后放疗组的5年OS、DFS和局部无复发生存期均呈现增加趋势。Abrams等^[44]报告显示男性乳腺癌辅助放疗可改善淋巴结阳性患者的5年OS(1~3个淋巴结阳性组: 79% vs 72%, $P=0.05$; 4个及以上淋巴结阳性组: 73% vs 53%, $P<0.001$)。此外多项研究结果支持辅助放疗在局部控制和改善生存方面的作用^[44-48]。近年来,在女性乳腺癌中逐渐出现诸如大剂量低分割放疗、豁免局部辅助放疗、影像及计算机辅助精准放疗等创新,以提高精确性和减少心肺放疗毒性,但在男性乳腺癌中暂未有相关研究开展。目前术后辅助放疗在男性乳腺癌患者中通常未得到充分利用,平均利用率约为35%^[49]。然而,数据报告乳房切除术后放疗的使用率有增加的趋势(2004年为66%, 2014年为74.6%)^[5],伴随临床利用率提高,后续或可依据更多研究数据对辅助放疗作出详细推荐。

2.4 内分泌治疗

在男性乳腺癌中,99%的肿瘤雌激素受体阳性,82%孕激素受体阳性,9%HER-2阳性,0.3%为三阴性^[50]。由于绝大多数男性乳腺癌为激素受体阳性,因此内分泌治疗是男性乳腺癌治疗的重要组成部分。目前为止,他莫昔芬一直是女性乳腺癌和男性乳腺癌中使用最广泛的抗雌激素疗法,2023男乳指南也推荐他莫昔芬为激素受体阳性男性乳腺癌患者的首选药物。Eggemann等^[51]的前瞻性研究显示,与他莫昔芬治疗组相比,未接受他莫昔芬治疗组男性乳腺癌患者的DFS显著降低($P=0.002$),未接受他莫昔芬治疗和接受他

莫昔芬治疗的两组患者复发率或死亡率分别为22.6%和13.9%。但Oke等^[52]的研究发现老年男性乳腺癌患者及贫困地区的患者他莫昔芬依从性较低,且有研究显示他莫昔芬在治疗男性乳腺癌患者的前18个月发生血栓事件的风险明显增加^[53],上述问题在治疗决策及临床管理时应予以考虑。同时在结合循证医学证据的基础上2023男乳指南指出,适合辅助内分泌治疗但有他莫昔芬禁忌证的激素受体阳性男性乳腺癌患者可给予芳香化酶抑制剂+促性腺激素释放激素激动剂(gonadotropin-releasing hormone agonist, GnRH-a)。但值得注意的是,MALE II期临床试验结果显示他莫昔芬或芳香化酶抑制剂中联用GnRH-a会进一步抑制雌二醇水平,进而影响患者生活质量,使用时应仔细权衡GnRH-a可能带来的不良反应^[54]。美国临床肿瘤学会指南中推荐氟维司群作为晚期或转移性激素受体阳性、HER-2阴性男性乳腺癌的可用选择^[55],而2023男乳指南并未纳入常规推荐。此外,一些研究也证明依维莫司、Abemaciclib、周期蛋白依赖性激酶4/6抑制剂等在男性乳腺癌中同样有一定疗效且耐受良好^[56-58],但纳入患者数量较少,缺乏有力证据支持。

2.5 抗雄治疗

近年,靶向雄激素受体的疗法也有望成为男性乳腺癌潜在的治疗方法。研究^[59]显示,男性乳腺癌患者接受比卡鲁胺加戈舍瑞林抗雄激素治疗,肿瘤可于影像学上保持4个月无进展,并且耐受性良好,未见报告的副作用。另有研究^[60]指出雄激素受体抑制剂恩杂鲁胺及Seviteronel在两性乳腺癌中有良好效用。但由于目前抗雄激素药物的证据大多来自小样本的研究,加之男性乳腺癌患者中雄激素受体的阳性率还尚未统一,雄激素受体治疗的效用有待进一步探究。

2.6 辅助治疗

目前关于男性乳腺癌的辅助治疗报道很少,方案多参照于女性乳腺癌。男性乳腺癌化疗方案以多西他赛+环磷酰胺或多柔比星+环磷酰胺,联合或不联合紫杉醇方案为主^[61]。在II期和III期男性乳腺癌中,蒽环类+紫杉类药物组合可降低复发,改善OS^[49]。HER-2阳性男性乳腺癌患者可进行曲妥珠单抗和(或)帕妥珠单抗靶向治疗^[62]。鉴于男性乳腺癌中BRCA基因突变的频率,多腺

苷二磷酸核糖聚合酶抑制剂也有一定应用价值。

3 总结与展望

男性乳腺癌发病率低,但初诊时多较晚,生存获益明显低于女性乳腺癌,与女性相比,男性患者在所有阶段的死亡率均更高^[63]。尽管常见的女性乳腺癌治疗策略适用于男性乳腺癌的管理,但男性乳腺癌与女性乳腺癌的生物学特性存在明显差异。近年越来越多的针对乳腺癌的大型研究开始纳入符合条件的男性患者,但仍有必要增加专门针对男性乳腺癌的相关研究,尤其内分泌治疗最佳方案、新型靶向药物等的相关研究。2023男乳指南作为中国第一部男性乳腺癌临床实践指南将为男性乳腺癌患者的及时识别、提升健康管理水平提供重要依据,并对推动相关知识普及、提高男性健康意识产生积极意义。但目前限于男性乳腺癌的认知水平与研究数据,仍需要继续开展前瞻性研究以及建立和完善成熟、可靠的治疗策略选择体系。

参考文献

- [1] Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2021[J]. CA: A Cancer Journal for Clinicians, 2021, 71(1): 7-33.
- [2] 中华医学会外科学分会乳腺外科学组. 中国男性乳腺癌临床诊治实践指南(2023版)[J]. 中国实用外科杂志, 2023, 43(2): 139-143.
- [3] Accomasso F, Actis S, Minella C, et al. Clinical, pathological, and prognostic features of male breast cancer: A multi-center study[J]. Current Oncology, 2023, 30(11): 9860-9871.
- [4] Cardoso F, Bartlett JMS, Slaets L, et al. Characterization of male breast cancer: Results of the EORTC 10085/TBCRC/BIG/NABCG international male breast cancer program[J]. Annals of Oncology: Official Journal of the European Society for Medical Oncology, 2018, 29(2): 405-417.
- [5] Yadav S, Karam D, Bin Riaz I, et al. Male breast cancer in the United States: Treatment patterns and prognostic factors in the 21st century[J]. Cancer, 2020, 126(1): 26-36.
- [6] Xi Lei, Zhou Jinxing, Wu Yan, et al. Clinicopathological features and correlation analysis of male breast cancer[J]. Medicine, 2023, 102(30): e34408.
- [7] McFarland BJ, Luo Alan, Wang Xiaoqin. Male breast cancer: Report of two cases with bloody nipple discharge[J]. Radiology Case Reports, 2023, 18(9): 3323-3330.

- [8] Salih AM, Hammood ZD, Kakamad FH, et al. Paget's disease of the breast in male with underlying invasive ductal carcinoma: A case report with review of literature[J]. *Annals of Medicine and Surgery*, 2021, 72: 103035.
- [9] Koseci T, Haksöyler V, Olgun P, et al. Male breast cancer: Clinical, demographical, and pathological features in a cohort of 41 patients[J]. *Cureus*, 2021, 13(9): e17812.
- [10] Wang Bo, Wang Li, Zhao Zhenya, et al. Cystic encapsulated papillary carcinoma with ductal carcinoma in situ in the male breast: A clinicopathologic feature with a diagnostic challenge: A case report and review of literature[J]. *Medicine*, 2023, 102(44): e34388.
- [11] Wong WG, Perez Holguin RA, Kanwar R, et al. Management of male patients with occult breast cancer: Analysis of the national cancer database[J/OL]. *The Journal of Surgical Research*, 2023: 1-8[2023-10-15]. <https://pubmed.ncbi.nlm.nih.gov/37839100/>.
- [12] Rong Xueyu, Zhu Qiang, Jia Wenxiu, et al. Ultrasonographic assessment of male breast diseases[J]. *The Breast Journal*, 2018, 24(4): 599-605.
- [13] Gao Yiming, Goldberg JE, Young TK, et al. Breast cancer screening in high-risk men: A 12-year longitudinal observational study of male breast imaging utilization and outcomes[J]. *Radiology*, 2019, 293(2): 282-291.
- [14] Healy NA, Parag Y, Wallis MG, et al. Outcomes of male patients attending the symptomatic breast unit: adherence to local and national imaging guidelines and effectiveness of clinical examination and imaging in detecting male breast cancer[J]. *Clinical Radiology*, 2022, 77(1): e64-e74.
- [15] Ryu SW, Ho K, O'Toole SA, et al. Case report of male breast cancer detected on magnetic resonance imaging[J]. *Journal of Medical Imaging and Radiation Oncology*, 2017, 61(3): 369-371.
- [16] Abunimer L, O'Brien SR, Calisi N. Male breast imaging uncovers lymphoma[J]. *Journal of Radiology Case Reports*, 2023, 17(2): 1-8.
- [17] Sharma S, Fischer A, Hatch P, et al. A case of bilateral male breast cancer- What does it teach us?[J]. *Radiology Case Reports*, 2023, 18(4): 1592-1595.
- [18] Ogura K, Shibasaki Y, Honda S, et al. Retiform hemangioendothelioma of the breast in a man with (18)F-fluorodeoxyglucose accumulation on positron emission tomography: A case report[J]. *Surgical Case Reports*, 2023, 9(1): 53.
- [19] Fang Ming, Liu Guilin, Luo Guoliang, et al. Feasibility and safety of image-guided vacuum-assisted breast biopsy: A PRISMA-compliant systematic review and meta-analysis of 20 000 population from 36 longitudinal studies[J]. *International Wound Journal*, 2019, 16(6): 1506-1512.
- [20] Hoda RS, Arpin Iii RN, Gottumukkala RV, et al. Diagnostic value of fine-needle aspiration in male breast lesions[J]. *Acta Cytologica*, 2019, 63(4): 319-327.
- [21] Yang Yinlong, Li Shiping, Liu Guangyu, et al. Is core needle biopsy effective at diagnosing male breast lesions[J]. *Breast Cancer Research and Treatment*, 2019, 177(2): 507-511.
- [22] Nofal MN, Yousef AJ. The diagnosis of male breast cancer[J]. *The Netherlands Journal of Medicine*, 2019, 77(10): 356-359.
- [23] Huang Conggai, Li Mengze, Wang Shaohua, et al. The application of fine needle aspiration biopsy in the diagnosis of axillary masses[J]. *Acta Cytologica*, 2021, 65(3): 213-219.
- [24] Fujioka T, Mori M, Kubota K, et al. Clinical usefulness of ultrasound-guided fine needle aspiration and core needle biopsy for patients with axillary lymphadenopathy[J]. *Medicina*, 2021, 57(7): 722.
- [25] Al Saati A, Vande Perre P, Pleneccagnies J, et al. Multi-gene panel sequencing identifies a novel germline mutation profile in male breast cancer patients[J]. *International Journal of Molecular Sciences*, 2023, 24(18): 14348.
- [26] Barnes DR, Silvestri V, Leslie G, et al. Breast and prostate cancer risks for male BRCA1 and BRCA2 pathogenic variant carriers using polygenic risk scores[J]. *JNCI: Journal of the National Cancer Institute*, 2021, 114(1): 109-122.
- [27] McClurg DP, Urquhart G, McGoldrick T, et al. Analysis of the clinical advancements for BRCA-related malignancies highlights the lack of treatment evidence for BRCA-positive male breast cancer[J]. *Cancers*, 2022, 14(13): 3175.
- [28] Doğan İ, Aydın E, Yazıcı H, et al. Comparison of clinical, pathological, and prognostic features in BRCA mutant and wild-type male breast cancer patients[J]. *European Journal of Breast Health*, 2022, 18(4): 323-328.
- [29] Daly MB, Pal T, Berry MP, et al. Genetic/familial high-risk assessment: breast, ovarian, and pancreatic, version 2.2021, NCCN clinical practice guidelines in oncology[J]. *Journal of the National Comprehensive Cancer Network*, 2021, 19(1): 77-102.
- [30] Tutt ANJ, Garber JE, Kaufman B, et al. Adjuvant olaparib for patients with BRCA1-or BRCA2-mutated breast

- cancer[J]. New England Journal of Medicine, 2021, 384(25): 2394-2405.
- [31] Kurian AW, Abrahamse P, Furgal A, et al. Germline genetic testing after cancer diagnosis[J]. JAMA, 2023, 330(1): 43-51.
- [32] Allen I, Hassan H, Sofianopoulou E, et al. Risk of developing a second primary cancer in male breast cancer survivors: A systematic review and Meta-analysis[J]. British Journal of Cancer, 2022, 127(9): 1660-1669.
- [33] Bucalo A, Conti G, Valentini V, et al. Male breast cancer risk associated with pathogenic variants in genes other than *BRCA1/2*: An Italian case-control study[J]. European Journal of Cancer, 2023, 188: 183-191.
- [34] 中国临床肿瘤学会指南工作委员会. 中国临床肿瘤学会(CSCO)乳腺癌诊疗指南 2023[M]. 北京: 人民卫生出版社, 2023.
- [35] Schiza A, Fredriksson I, Sund M, et al. Treatment utilization and effectiveness of neoadjuvant chemotherapy comparing men and women diagnosed with breast cancer: A Swedish retrospective cohort study[J/OL]. Breast Cancer Research And Treatment, 2023: 1-9[2023-10-19]. <https://pubmed.ncbi.nlm.nih.gov/37812362/>.
- [36] Cao L, Hue JJ, Freyvogel M, et al. Despite equivalent outcomes, men receive neoadjuvant chemotherapy less often than women for lymph node-positive breast cancer[J]. Annals of Surgical Oncology, 2021, 28(11): 6001-6011.
- [37] Leone JP, Hassett MJ, Leone J, et al. Efficacy of neoadjuvant chemotherapy in male breast cancer compared with female breast cancer[J]. Cancer, 2022, 128(21): 3796-3803.
- [38] Leone JP, Freedman RA, Leone J, et al. Survival in male breast cancer over the past 3 decades[J]. JNCI: Journal of the National Cancer Institute, 2023, 115(4): 421-428.
- [39] Giordano SH. Breast cancer in men[J]. New England Journal of Medicine, 2018, 378(24): 2311-2320.
- [40] Lin AP, Huang TW, Tam KW. Treatment of male breast cancer: Meta-analysis of real-world evidence[J]. The British Journal of Surgery, 2021, 108(9): 1034-1042.
- [41] Sauder CAM, Bateni SB, Davidson AJ, et al. Breast conserving surgery compared with mastectomy in male breast cancer: A brief systematic review[J]. Clinical Breast Cancer, 2020, 20(3): e309-e314.
- [42] Shang Qingyao, Feng Kexin, Wei Ya, et al. Evaluation of male breast cancer and the application of sentinel lymph node biopsy: A multicenter retrospective study[J]. Oncologist, 2023, 28(12): e1170-e1178.
- [43] Chung SH, de Geus SWL, Shewmaker G, et al. Axillary lymph node dissection is associated with improved survival among men with invasive breast cancer and sentinel node metastasis[J]. Annals of Surgical Oncology, 2023, 30(9): 5610-5618.
- [44] Abrams MJ, Koffer PP, Wazer DE, et al. Postmastectomy radiation therapy is associated with improved survival in node-positive male breast cancer: A population analysis[J]. International Journal of Radiation Oncology, Biology, Physics, 2017, 98(2): 384-391.
- [45] Bakalov V, Jayakrishnan TT, Abel S, et al. The use of adjuvant radiation therapy in male breast cancer and its impact on outcomes[J]. Cancer Treatment and Research Communications, 2021, 27: 100359.
- [46] Forster T, Köhler C, El Shafie R, et al. Adjuvant radiation therapy for male breast cancer-A rare indication?[J]. Cancers, 2020, 12(12): 3645.
- [47] Jardel P, Vignot S, Cutuli B, et al. Should adjuvant radiation therapy be systematically proposed for male breast cancer? A systematic review[J]. Anticancer Research, 2018, 38(1): 23-31.
- [48] Wu Peiwen, He Dongjie, Zhu Shuchai, et al. The role of postoperative radiation therapy in stage I-III male breast cancer: A population-based study from the surveillance, epidemiology, and end results database[J]. Breast, 2022, 65: 41-48.
- [49] Zheng Guoliang, Leone JP. Male breast cancer: An updated review of epidemiology, clinicopathology, and treatment[J]. Journal of Oncology, 2022, 2022: 1734049.
- [50] Cardoso F, Paluch-Shimon S, Senkus E, et al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5)[J]. Annals of Oncology: Official Journal of the European Society for Medical Oncology, 2020, 31(12): 1623-1649.
- [51] Eggemann H, Brucker C, Schrauder M, et al. Survival benefit of tamoxifen in male breast cancer: prospective cohort analysis[J]. British Journal of Cancer, 2020, 123(1): 33-37.
- [52] Oke O, Niu Jiangong, Chavez-MacGregor M, et al. Adjuvant tamoxifen adherence in men with early-stage breast cancer[J]. Cancer, 2022, 128(1): 59-64.
- [53] Eggemann H, Bernreiter AL, Reinisch M, et al. Tamoxifen treatment for male breast cancer and risk of thromboembolism: Prospective cohort analysis[J]. British Journal of Cancer, 2019, 120(3): 301-305.
- [54] Reinisch M, Seiler S, Hauzenberger T, et al. Efficacy of endocrine therapy for the treatment of breast cancer in men: Results from the male phase 2 randomized clinical trial[J]. JAMA Oncology, 2021, 7(4): 565-572.

- [30] Lai YT, Chao HW, Lai AC, et al. CPEB2-activated PDGFR α mRNA translation contributes to myofibroblast proliferation and pulmonary alveologenesis[J]. *Journal of Biomedical Science*, 2020, 27(1): 52.
- [31] Metelo-Coimbra C, Roncon-Albuquerque R. Artificial placenta: Recent advances and potential clinical applications[J]. *Pediatric Pulmonology*, 2016, 51(6): 643-649.
- [32] Kapoor V, Malviya MN, Soll R. Lipid emulsions for parenterally fed preterm infants[J]. *Cochrane Database of Systematic Reviews*, 2019, 6(6): D13163.
- [33] Harvey SL, Fallon BP, McLeod JS, et al. Hepatic function in premature lambs supported by the artificial placenta and total parenteral nutrition[J]. *American Society for Artificial Internal Organs*, 2022, 68(7): 949-955.
- [34] 蓝思源, 洪莉. 早产儿宫外生长发育迟缓的研究进展[J]. *国际儿科学杂志*, 2022, 49(3): 149-153.
- [35] 唐建明, 陈冠初, 谈笑, 等. 早期高血糖与极低出生体重儿主要并发症及病死率的关系[J]. *兰州大学学报: 医学版*, 2022, 48(7): 71-76.
- [36] Panero AJ, Hirahara AM, Andersen WJ, et al. Are amniotic fluid products stem cell therapies? A study of amniotic fluid preparations for mesenchymal stem cells with bone marrow comparison[J]. *The American Journal of Sports Medicine*, 2019, 47(5): 1230-1235.
- [37] Ozek E, Kersin SG. Intraventricular hemorrhage in preterm babies[J]. *Turkish Archives of Pediatrics*, 2020, 55(3): 215-221.
- [38] Ozawa K, Davey MG, Tian Z, et al. Fetal echocardiographic assessment of cardiovascular impact of prolonged support on EXTrauterine environment for neonatal development (EXTEND) system[J]. *Ultrasound in Obstetrics & Gynecology*, 2020, 55(4): 516-522.
- [39] 刘诗月, 史源. 人造子宫在超早产儿救治中的研究进展[J]. *中国实用儿科杂志*, 2021, 36(2): 147-151.
- [40] Mercurio MR. The EXTEND system for extrauterine support of extremely premature neonates: Opportunity and caution[J]. *Pediatric Research*, 2018, 84(6): 795-796.
- [41] 王刚, 李秋平, 洪小杨, 等. 人工胎盘的研究进展与临床转化的挑战[J]. *中国实用儿科杂志*, 2023, 38(2): 103-108.
- [42] Kukora SK, Mychaliska GB, Weiss EM. Ethical challenges in first-in-human trials of the artificial placenta and artificial womb: Not all technologies are created equally, ethically[J]. *Journal of Perinatology*, 2023, 43(11): 1337-1342.

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- [55] Brackstone M, Baldassarre FG, Perera FE, et al. Management of the axilla in early-stage breast cancer: Ontario health (cancer care ontario) and ASCO guideline[J]. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, 2021, 39(27): 3056-3082.
- [56] Johnston SRD, Harbeck N, Hegg R, et al. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE)[J]. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, 2020, 38(34): 3987-3998.
- [57] Yıldırım H, Mutlu E, Chalabiyev E, et al. Clinical outcomes of cyclin-dependent kinase 4-6 (CDK 4-6) inhibitors in patients with male breast cancer: A multicenter study[J]. *Breast*, 2022, 66: 85-88.
- [58] Vasconcelos de Matos L, Volovat S, Debiase M, et al. Unfolding the role of the PI3K/AKT/MTOR pathway in male breast cancer: A pragmatic appraisal[J]. *Breast*, 2023, 72: 103576.
- [59] Wang Xinhua, Zhang Jing, Wu Jie, et al. Case report: Response to immunotherapy and anti-androgen therapy in male occult triple-negative breast cancer[J]. *Frontiers in Oncology*, 2022, 12: 840453.
- [60] Chatterji S, Krzoska E, Thoroughgood CW, et al. Defining genomic, transcriptomic, proteomic, epigenetic, and phenotypic biomarkers with prognostic capability in male breast cancer: A systematic review[J]. *The Lancet. Oncology*, 2023, 24(2): e74-e85.
- [61] PDQ Adult Treatment Editorial Board. Male breast cancer treatment (PDQ®): Health professional version[M]. Bethesda: National Cancer Institute, 2023.
- [62] Hassett MJ, Somerfield MR, Baker ER, et al. Management of male breast cancer: ASCO guideline[J]. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, 2020, 38(16): 1849-1863.
- [63] Wang Fei, Shu Xiang, Meszoely I, et al. Overall mortality after diagnosis of breast cancer in men vs women[J]. *JAMA Oncology*, 2019, 5(11): 1589-1596.

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