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关于呼吸机相关性肺炎的文献计量学和研究热点

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摘　要

呼吸机相关性肺炎(ventilator-associated pneumonia, VAP)是医院常见的获得性感染，是ICU内重症患者死亡的诱因之一。本研究旨在探讨过去已发表的文章，采用文献计量学方法和可视化分析来探索该领域的发展趋势和热点。方法：我们从SCI-Expanded of WoSCC中检索了过去十多年期间收录的关于呼吸机相关性肺炎所有文章，利用CiteSpace、bibliometrix和VOSviewer软件包分析文献计量数据。结果：共检索到1474篇文章，来自82个国家，其中“美国”以355篇文章位居第一，其次是中国(253篇)。“University of Barcelona”是最主要的学术机构，该研究主要发表在“Critical Care”等专业期刊上，“Torres A”以31篇已发表的出版物被评为最具生产力的作者。“mechanical ventilation”、“mortality”、“risk factors”、“acinetobacter baumannii”是最常见的关键词，“cefliderocol”、“COVID-19”“carbapenem-resistant acinetobacter baumannil”是近年来的研究热点。结论：通过本研究为全面理解呼吸机相关性肺炎提供了客观依据，不断开发、研究新的抗生素仍是当下重中之重，更好地完善治疗策略来改善临床结局。

关键词

呼吸机相关性肺炎，Bibliometrics, CiteSpace, VOSviewers

Bibliometrics and Research Hotspots on Ventilator-Associated Pneumonia

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Abstract

Ventilator-associated pneumonia (VAP) is a common acquired infection in hospitals and one of the causes of death in critically ill patients in the ICU. This study aims to explore the development trends and hotspots in this field by reviewing previously published articles using bibliometric methods and visual analysis. Methods: We retrieved all the articles on ventilator-associated pneumonia included in SCI-Expanded of WoSCC over the past decade, and analyzed the bibliometric data using the CiteSpace, bibliometrix, and VOSviewer software packages. Results: A total of 1474 articles were retrieved, coming from 82 countries. The United States ranked first with 355 articles, followed by China with 253. "University of Barcelona" is the most important academic institution. The research was mainly published in professional journals such as "Critical Care". "Torres A" is the most productive author with 31 published papers. The most common keywords are "mechanical ventilation", "mortality", "risk factors", and "Acinetobacter baumannii". "Cefiderocol", "COVID-19", and "carbapenem-resistant Acinetobacter baumannii" have been research hotspots in recent years. Conclusion: This study provides an objective basis for a comprehensive understanding of ventilator-associated pneumonia, and the continuous development and research of new antibiotics remains a top priority. It is crucial to better refine treatment strategies to improve clinical outcomes.

Keywords

Ventilator-Associated Pneumonia, Bibliometrics, CiteSpace, VOSviewers

1. 引言

呼吸机相关性肺炎(VAP)是指气管插管或气管切开患者在接受机械通气 48 小时内肺实质感染[1]。撤机、拔管 48 小时内出现的肺炎，也属于 VAP。根据患者人群不同及诊断标准的差异，国外 ICU 中 VAP 的发生率为 4%~42%不等[2]-[8]。根据 VAP 发生时间的早晚分为早发现 VAP (机械通气 4 天内)和晚发性 VAP (机械通气 5 天后) [9]。感染是 VAP 患者死亡的原因之一，占三分之一到一半，革兰氏阴性杆菌患者病死率明显高于革兰氏阳性致病菌，其中早发性 VAP 的致病菌主要是嗜血杆菌、链球菌和甲氧西林敏感的金黄色葡萄球菌，晚发性 VAP 通常是由铜绿假单胞菌、不动杆菌属、肺炎克雷伯菌等多重耐药菌引起的[2] [10] [11]。抗生素的大量使用导致多重耐药病原体的不断发生[12]。VAP 与住院时间延长、机械通气时间以及医疗费用、死亡率增加有关[8]。抗生素的不正确使用增加了死亡风险，因此，初始抗生素的选择至关重要[13]。如果治疗不当，VAP 可导致严重的急性呼吸窘迫综合征或感染性休克[14]。而目前临床上诊断 VAP 尚未有很准确的定义，所以尽早地识别 VAP 至关重要。诊断 VAP 主要基于两个方面：一是依据病史、体格检查、白细胞增多、影像学改变；二是病原学检查，包括气管内抽吸物和支气管镜样本培养(保护标本刷、支气管肺泡灌洗液)阳性。其中最流行的临床肺部感染评分(CPIS)，该评分包括 6 个变量(体温、血白细胞、气管分泌物、氧合指数、胸部 X 线和革兰氏染色气管吸出物的半定量培养)，评分高于 6 分的患者有发生 VAP 的风险[15]-[18]。但由于各家医院诊断标准和参考方法的不同，VAP 的治疗仍是一大难题。尽管病原微生物学被认为是一种可行的标志物，但在 VAP 的诊断和预后来说有待商榷[19]。文献计量学是研究文献的数量特征及其变化规律的学科，主要通过定量分析的方法来评估和描述文

献的生产、传播和使用情况。它涉及对文献的统计分析，包括出版物的数量、引用情况、关键词等。文献计量学的研究可以帮助学者了解某一领域的发展趋势、研究热点。本研究旨在分析 VAP 的研究现状，为将来进一步探索 VAP 提供客观依据。

2. 材料与方法

2.1. 数据来源与检索方法

Web of Science 核心合集(WoSCC)的 Science Citation Index Expanded 是引文数据的主要来源，所有数据均由两位作者独立完成，检索数据策略包括 TI = “ventilator-associated pneumonia” AND Document types = (ARTICLE OR REVIEW) AND Language = “(English)”，病例报告、会议摘要、社论材料和其他文件类型被排除在外。检索的结果以“纯文本文件”导出，记录内容选择“全记录和被引参考文献”，文献的纳入和排除过程如图 1 所示。

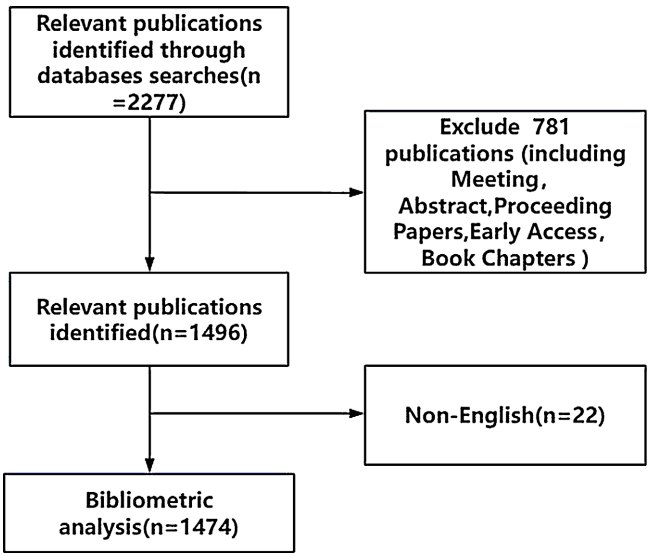


Figure 1. Flowchart of the screening process
图 1. 筛选过程流程图

2.2. 数据分析

所有下载的文献导入到 Vosviewer、Citespace、bibliometrix 进行进一步的分析。Vosviewer 是一种基于网络数据创建和探索地图的软件工具，可用于探索合著、共现、引文、书目耦合和共同引文链接：网络、叠加或密度可视化[20]。Bibliometrix 于 2017 年由 Massimo Aria 博士和 Corrado Cuccurullo 博士推出[21]，是一个全面的映射分析工具，需要有 R 语言的知识，其支持文献计量分析过程的三个阶段：(a) 数据导入和转换为 R 格式；(b) 数据集的文献计量分析和(c) 矩阵的构建[22]。在本研究中，被用于(a) 对国家/地区之间的合作及出版物的分布；(b) 国家/地区之间的合作集群；(c) 关键词趋势主题的分析。CiteSpace 是 Chen 开发的基于 Java 的免费软件，是用于可视化和分析科学文献的最流行的文献计量工具之一，通常用于确定给定领域的知识结构、分布和演变[23]。在本研究中，CiteSpace 被用于(a) 对机构进行合作分析；(b) 分析作者的共被引关系；(c) 对科学期刊进行双地图叠加；(d) 对参考文献进行共引分析；(e) 确定引文爆发次数最强的前 20 篇参考文献。在网络图中，节点表示各种项目，例如机构、作者和参考文献。节点大小和色环分别表示这些项目的数量和不同的年份。节点之间的线条反映了项目的合作或共引关系[24]。

3. 结果

3.1. 概述

总体而言，我们从 WOSCC 中检索到 1474 篇关于 VAP 的研究，其中包括 1236 篇“articles”和 238 篇“reviews”，图 2 显示了 VAP 的年度出版物数量和每年的引用频次，由图可知，近十多年来发表的出版物逐年增加，2017 年共产出 123 篇，生产高峰出现在 2022 年，共发表 143 篇，近两年有所下降(2024 年数据未统计完全)，但目前关于 VAP 的研究仍是热点，总体而言，该领域呈增长趋势。

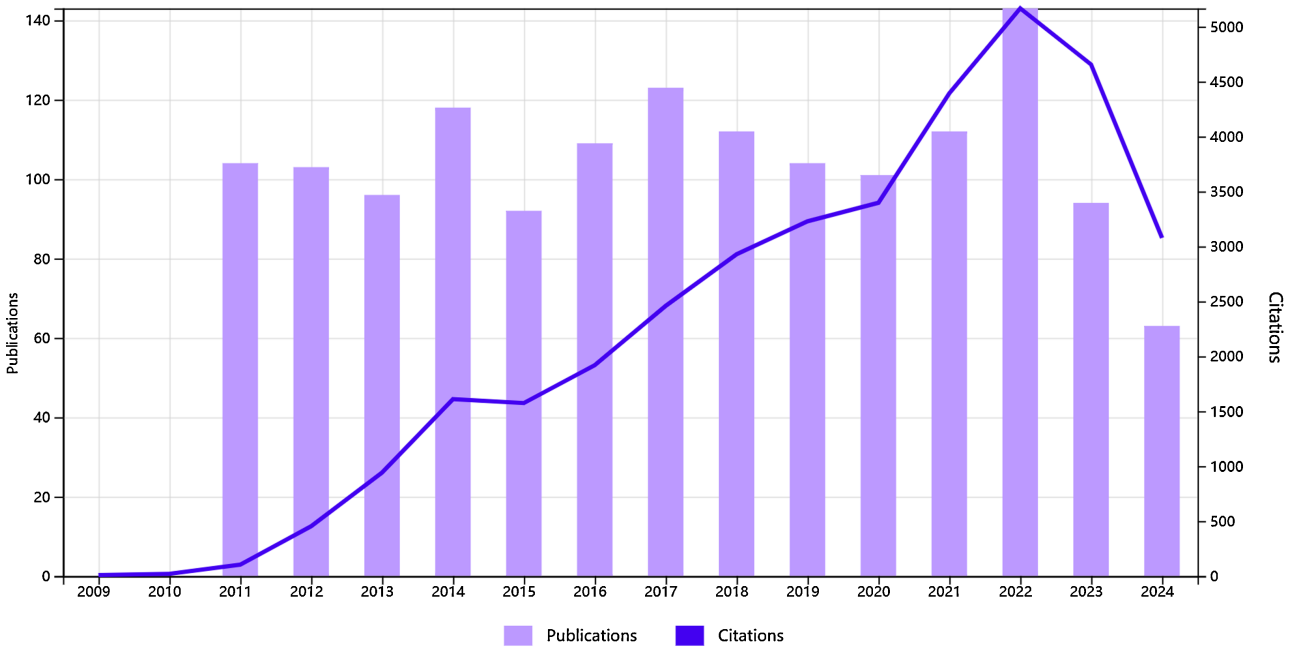


Figure 2. The annual publication of the ventilator-associated pneumonia and the citation frequency each year
图 2. VAP 的年度出版物及每年的引用频次

3.2. 主要国家和地区

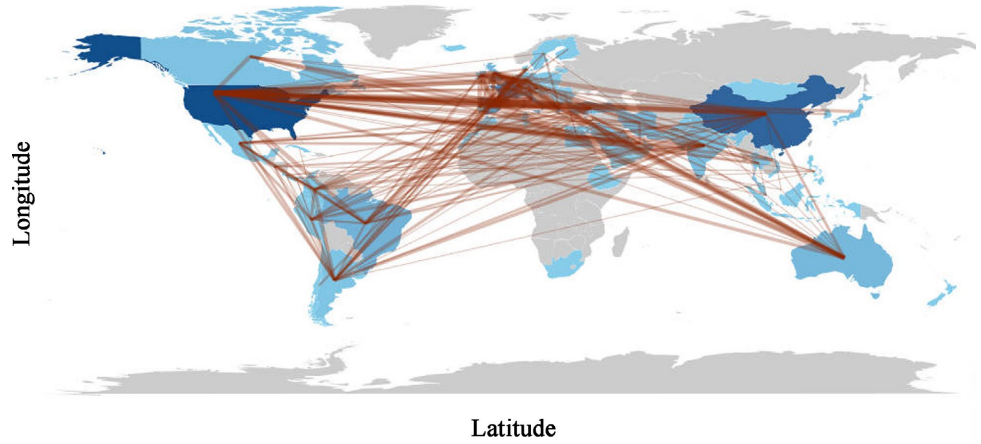
根据数据显示，2011 至 2024 年间，来自 82 个国家的学者对 VAP 的研究作出了贡献。如表 1 所示，美国(n = 355, 24.03%)是关于 VAP 出版数量最多的国家，其次是中国(n = 253, 17.12%)、法国(n = 188, 12.72%)。来自美国、中国和法国三个国家的出版物数量超过总数的一半(n = 53%)。亚洲与北美及西欧之间合作密切(图 3(a))。随后，我们对国家进行可视化，确定了一个协作集群(图 3(b))。由图可得知，不同国家之间进行了积极的合作。例如中国与美国、法国与西班牙之间合作紧密。

Table 1. Top Ten Countries and Institutions in ventilator-associated pneumonia Research
表 1. 研究呼吸机相关性肺炎前十名国家和机构

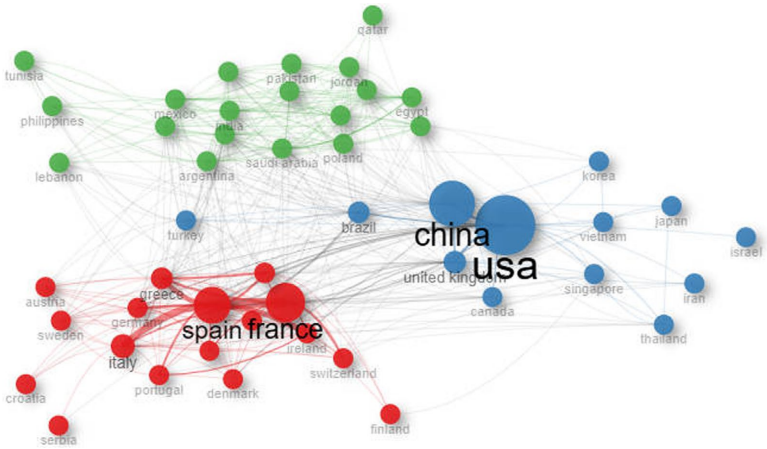
Country	Count	Institution	Count
USA	355	University of Barcelona	40
China	253	Autonomous University of Barcelona	25
France	188	Universite Paris Cite	24
Spain	133	University of Queensland	23

续表

Italy	80	University of Tennessee	23
Brazil	71	Brigham and Women's Hospital	22
Türkiye	62	Inserm	22
England	58	Washington University	22
Greece	55	Hospital Clinic De Barcelona	21
Australia	54	Sorbonne University	21



(a)



(b)

Figure 3. (a) Distribution of publications and cooperation between countries/region; (b) Cooperation clusters between countries/regions
图 3. (a) 出版物的分布和国家/地区之间的合作；(b) 国家/地区之间的合作集群

3.3. 活跃的机构和作者

排名前十的机构来自四个国家(表 1)，分别是美国(3/10)、法国(3/10)、西班牙(3/10)、澳大利亚(1/10)。西班牙的 University of Barcelona (n = 40)是生产力最高的机构，其次是 Autonomous University of Barcelona (n = 25)、Universite Paris Cite (n = 24)。随后，我们按照最少发表论文数等于 7 的标准选择了 95 家机构进行可视化，并根据各机构发表论文的数量和关系构建了协作网络(图 4)。图中的每个圆圈代表一个国家/地

区，圆圈的大小表示该国家/地区的出版物产出。圆圈之间的线条表示国家之间的合作，线条越宽表示合作越紧密。如图 4 所示，University of Barcelona 与 Washington University 之间合作紧密，University of Queensland 与 Autonomous University of Barcelona 之间关系密切。

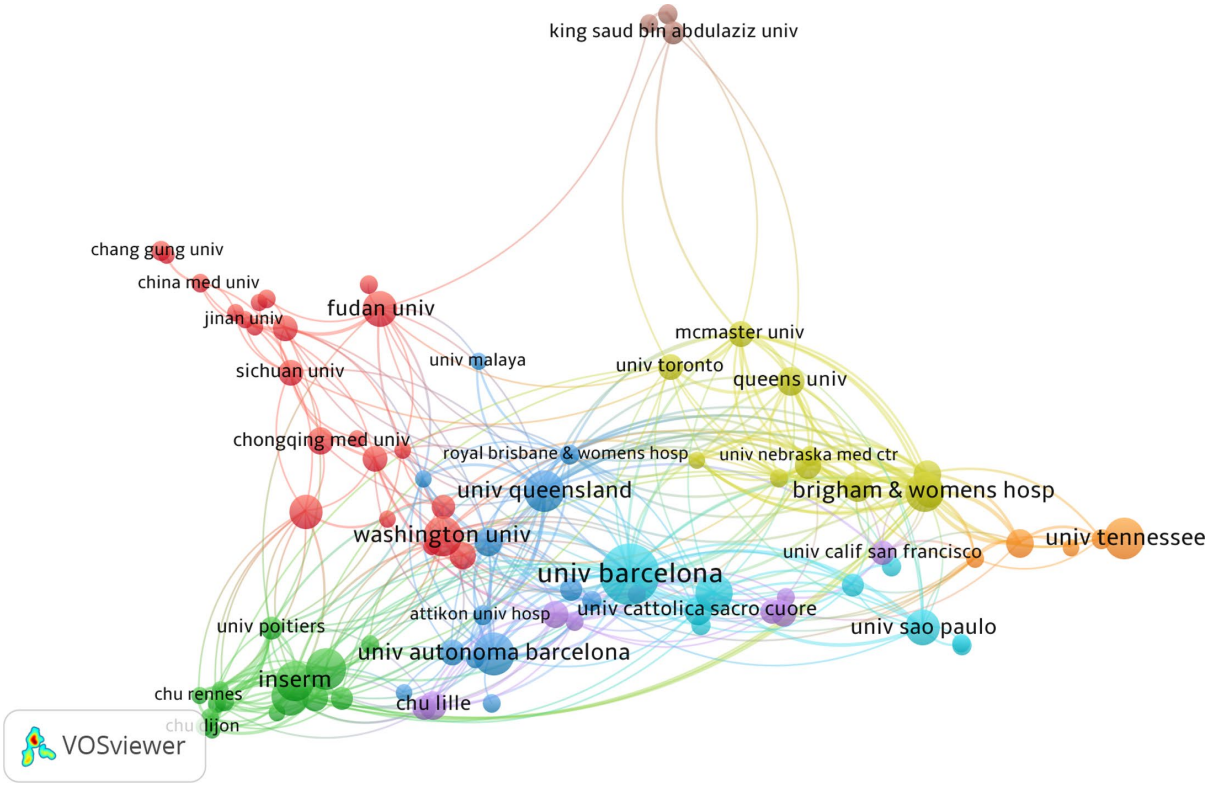


Figure 4. Visualization of research institutions
图 4. 研究机构可视化

3.4. 期刊与共同引用期刊

随后我们对已发表的期刊进行可视化分析(表 2)，得到以下几个结论：《Critical Care》是生产力最高的期刊(n = 53, 3.59%)，其次是《Journal of Critical Care》(n = 43, 2.91%)、《American Journal of Infection Control》(n = 43, 2.91%)和《Critical Care Medicine》(n = 31, 2.10%)。在排名前十的期刊中，影响因子最高的是《Intensive Care Medicine》(IF = 27.1)，随后是《Chest》(IF = 9.5)。最后，我们用 Vosviewer 将最小出版量等于 7 筛选了 52 种期刊，以绘制期刊网络图(图 5(a))。

共同引用分析旨在评估文章之间的关系。在共被引用的前十期刊中，被引次数超过 2000 次的期刊有 5 种，其中《Critical Care Medicine》是被引用次数最多的期刊(共被引次数为 3657)，《American Journal of Infection Control》(共被引次数为 2951)和《Intensive Care Medicine》(共被引次数为 2744)位于第二、第三。我们将最小共被引次数设置为 100 筛选出 70 种期刊，绘制网络图(图 5(b))。由图可知，Critical Care Medicine 与 Intensive Care Medicine、American Journal of Infection Control 之间有正向的引用关系。

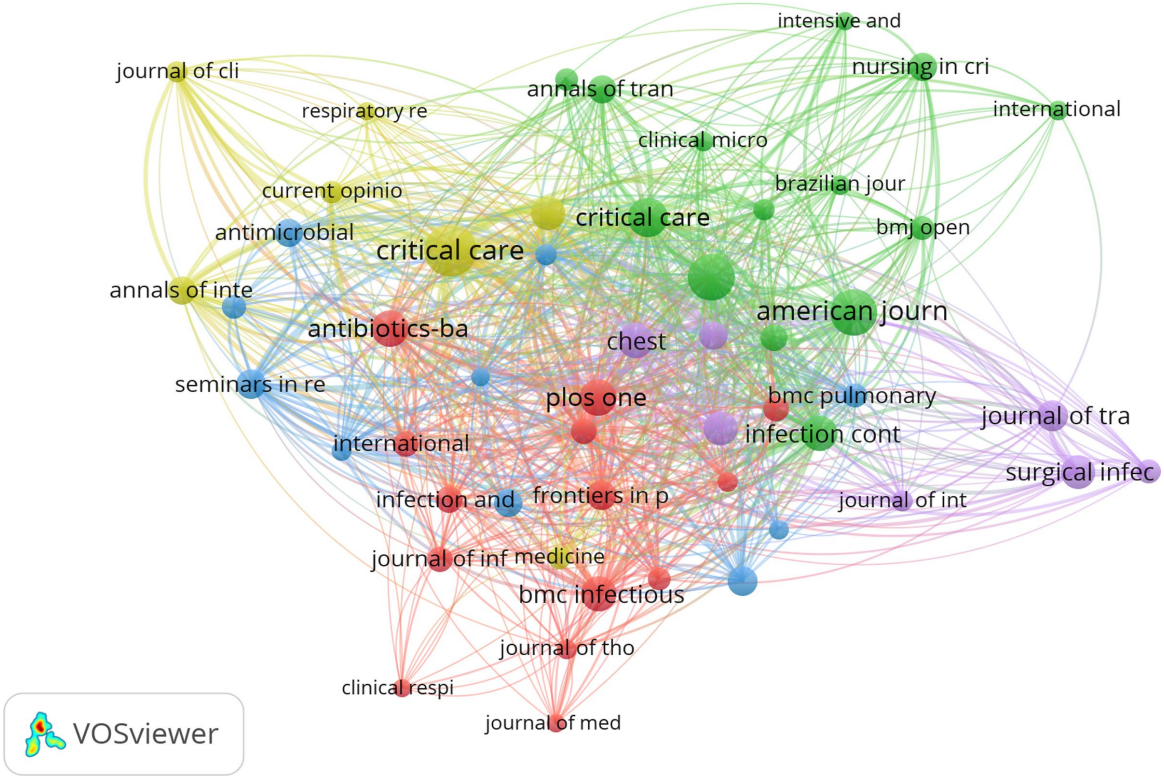
双映射叠加显示了期刊之间的多个域间连接(图 5(c))。图 5(c)中，左边的期刊是引用期刊，右边的期刊是被引用期刊；线条表示它们之间的引用关系。绿色的线条是主要引用途径。健康/护理/医学和分子/生物学/遗传学期刊中的出版物，大多被医学/医学/临床期刊中的出版物引用。

3.5. 作者及共同被引作者

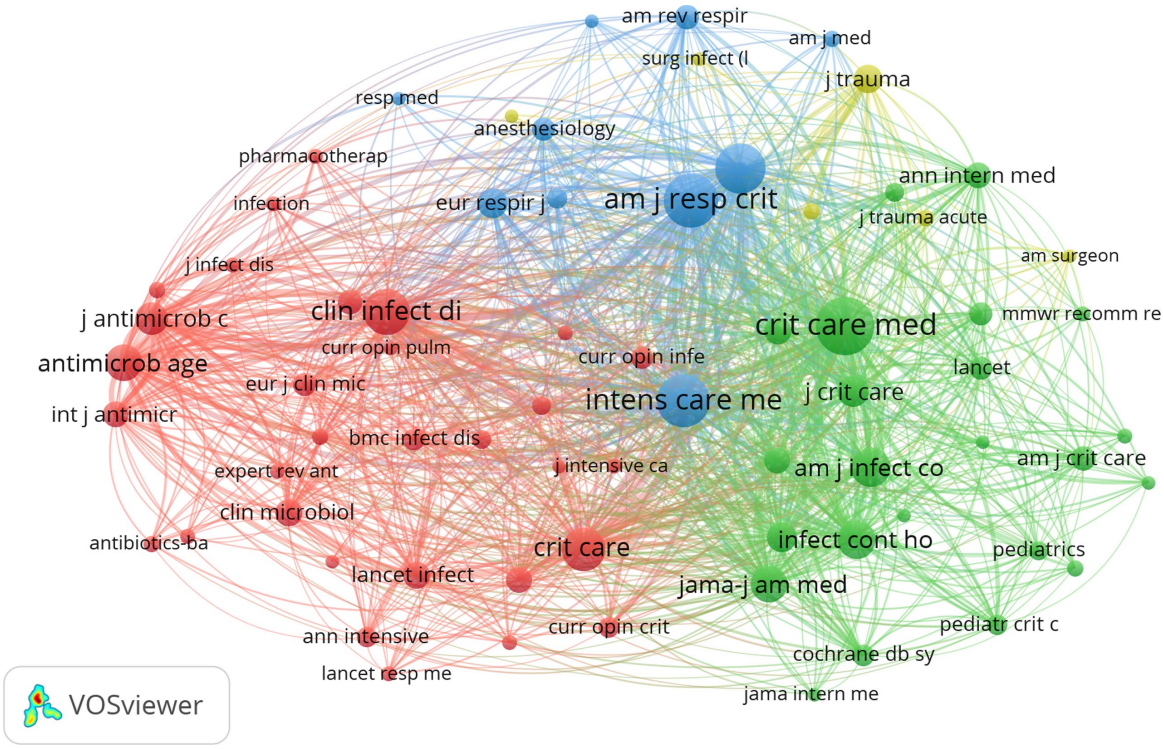
共有 7920 名作者参与了 VAP 的研究，其中 Torres A 以 31 篇文章位居首位(表 3)，其次是 Rello J (n = 24)、Martin-Loeches I (n = 22)。Klompas M 是总被引次数最多的作者(4159)。随后我们根据发表论文数大于等于 5 篇的作者构建了一个协作网络(图 6(a))，每个圆圈代表一位作者，圆圈之间的线条代表作者之间的联系，不同颜色的连接网络表示不同作者之间的合作集群。发表相关文章最多的作者节点最大。

Table 2. Contributions of the top 10 journals on VAP
表 2. 关于呼吸机相关性肺炎文献发表前十的期刊

Rank	Journal	Count (%)	Citation	IF
1	Critical Care	53 (3.59%)	2555	8.8
2	Journal of Critical Care	43 (2.91%)	863	3.2
3	American Journal of Infection Control	43 (2.91%)	819	3.8
4	Critical Care Medicine	31 (2.10%)	2049	7.7
5	Antibiotics-basel	26 (1.76%)	174	4.3
6	Plos One	26 (1.76%)	557	2.9
7	BMC Infectious Diseases	25 (1.69%)	569	3.4
8	Infection Control and Hospital Epidemiologgy	24 (1.62%)	1693	3.0
9	Chest	24 (1.62%)	1272	9.5
10	Intensive Care Medicine	22 (1.50%)	1484	27.1



(a)



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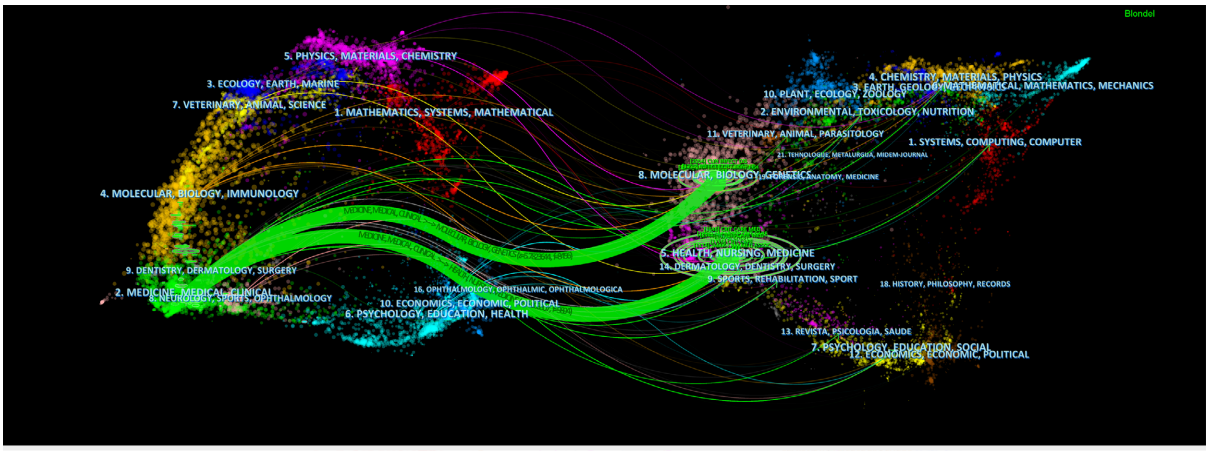


(c)

Figure 5. Ventilator-associated pneumonia research journal (a) and co-cited journals (b); Ventilator-associated pneumonia journal double figure overlay (c)
图 5. 关于 VAP 的研究期刊(a)与共被引期刊(b)；关于 VAP 的期刊双图叠加(c)

Table 3. Authors of the top ten published papers in ventilator-associated pneumonia research
表 3. 关于 VAP 研究发表论文前十的作者

Rank	Author	Publications	Citations
1	Torres A	31	1779
2	Rello J	24	854
3	Martin-Loeches I	22	1091

续表

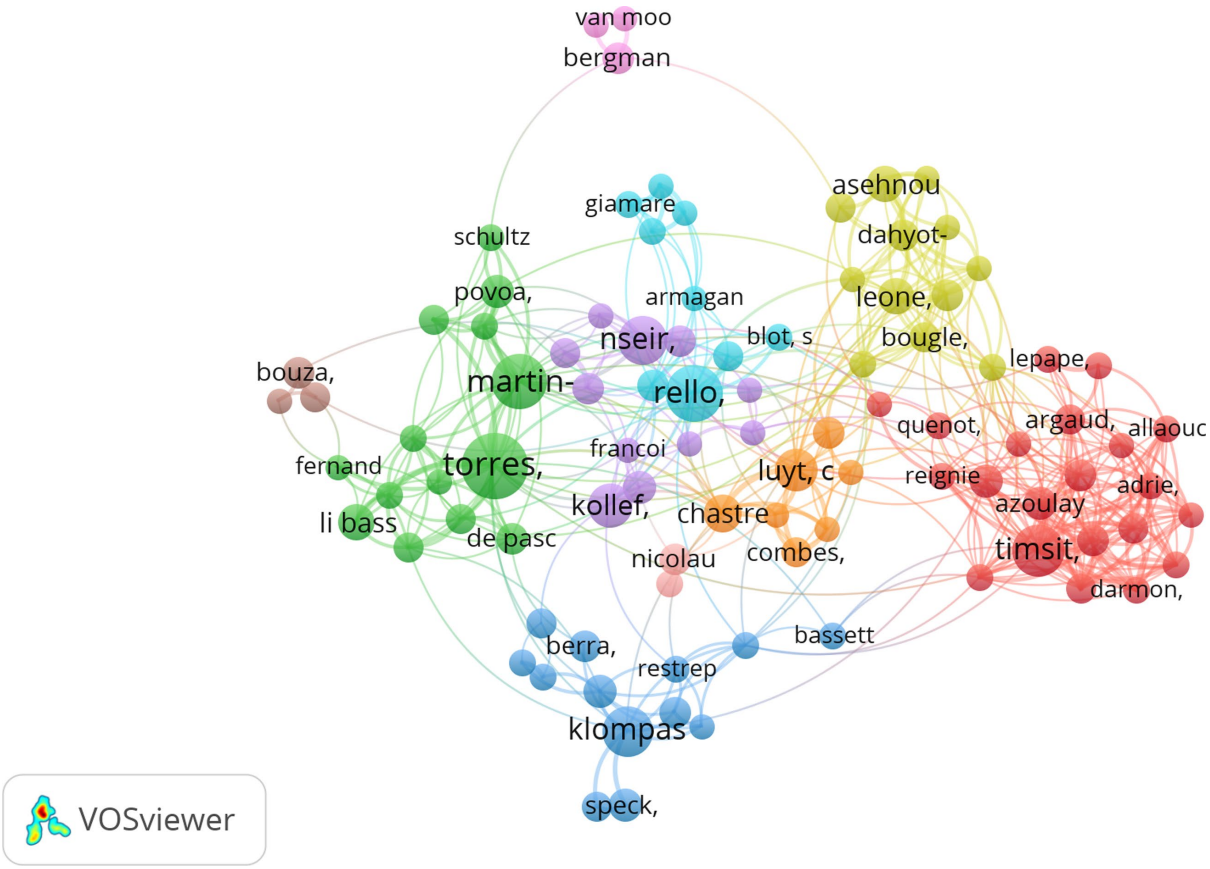
4	Timsit JF	20	1099
5	Klompas M	19	4159
6	Nseir S	18	361
7	Croce MA	17	193
8	Fabian TC	16	189
9	Swanson JM	15	150
10	Kollef MH	15	1154

此外，我们观察到多个作者之间的密切合作。例如，Torres A、Rello J、Martin-Loeches I 之间有着密切的合作。

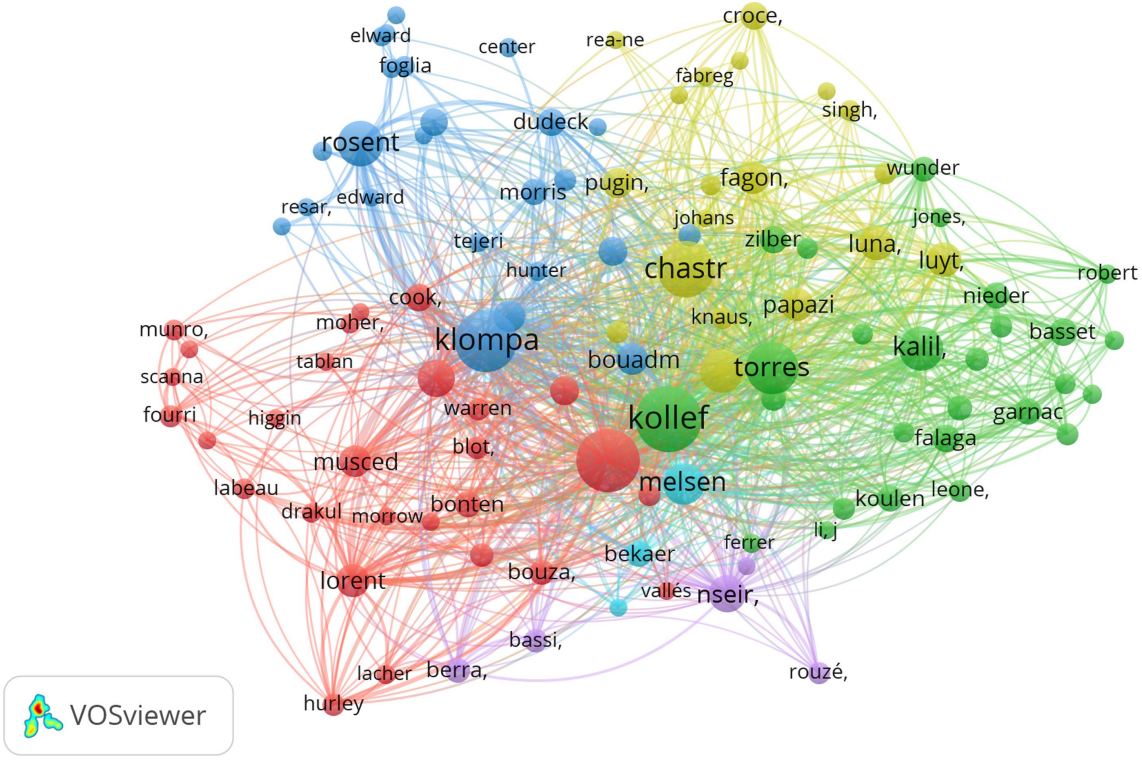
共被引作者是指两个或多个作者同时被另一篇或多篇论文引用，这两名或更多作者构成了共同被引关系(图 6(b))。如图所示，不同的共同被引作者之间也存在积极的合作，例如 Kollef MH 与 Klompas M, Torres A 之间都有密切的合作。

3.6. 共同引用的参考文献和参考文献突发

合引是指两篇或多篇文章同时被一篇或多篇论文引用，两篇文章视为合引关系[23] [25]。关于 VAP 的共被引文献有 24,863 篇，我们筛选共被引量大于等于 20 的文献构建共被引网络图(图 7)。由图可知，



(a)



(b)

Figure 6. Ventilator-associated pneumonia research authors (a) and co-cited authors (b)
图 6. 关于 VAP 的研究作者(a)和共同被引用作者(b)可视化

“[anonymous], 2005, am j resp crit care”与“chastre j, 2002, am j resp crit care”、“safdar n, 2005, crit care med”等文献存在密切的共被引关系。

带引文爆发的参考文献是指在一段时间内被某个领域的学者频繁引用的参考文献[25]。图 8 显示了引文爆发最稳健的前 20 篇参考文献。柱状图表示年份，红色柱状图表示强引文爆发度[26]。参考文献的引文爆发最早出现在 2008 年，具有最强引文爆发(强度 =41.91)的参考文献标题为“Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society”，是由 Andre C. Kalil 等人撰写的，引文爆发时间为 2017~2021 年。

3.7. 关键词和趋势主题

关键词是更深层次的总结。通过对关键词的分析，可以了解特定领域的研究热点，探索热点和研究方向[27]。我们通过 Vosviewer 对关键词进行聚类分析(图 9(a))，总共得到 4 个集群，代表了 4 个研究方向。节点之间的线越粗，关键字之间的联系就越强。其中蓝色簇中包括 ventilator-associated pneumonia、hospital-acquired pneumonia、therapy 等，红色簇中包括 intensive-care unit、mechanical ventilation 等，绿色簇中包括 diagnosis、morality 等，黄色簇中包括 impact、risk factors、prevention 等。关键词趋势主题表明了研究方向和研究领域，目前 VAP 的研究主要集中在 cefiderocol、carbapenem-resistant acinetobacter baumannii、COVID-19、acute respiratory distress syndrome 等。

采用文献计量学的方法，对检索到的 1474 篇文献进行分析，第一篇文章于 2011 年发表在《Critical Care》上，Zolfaghari [28]解释标准大容量低压套囊气管插管的固有设计缺陷是导致 VAP 的主要致病机制，

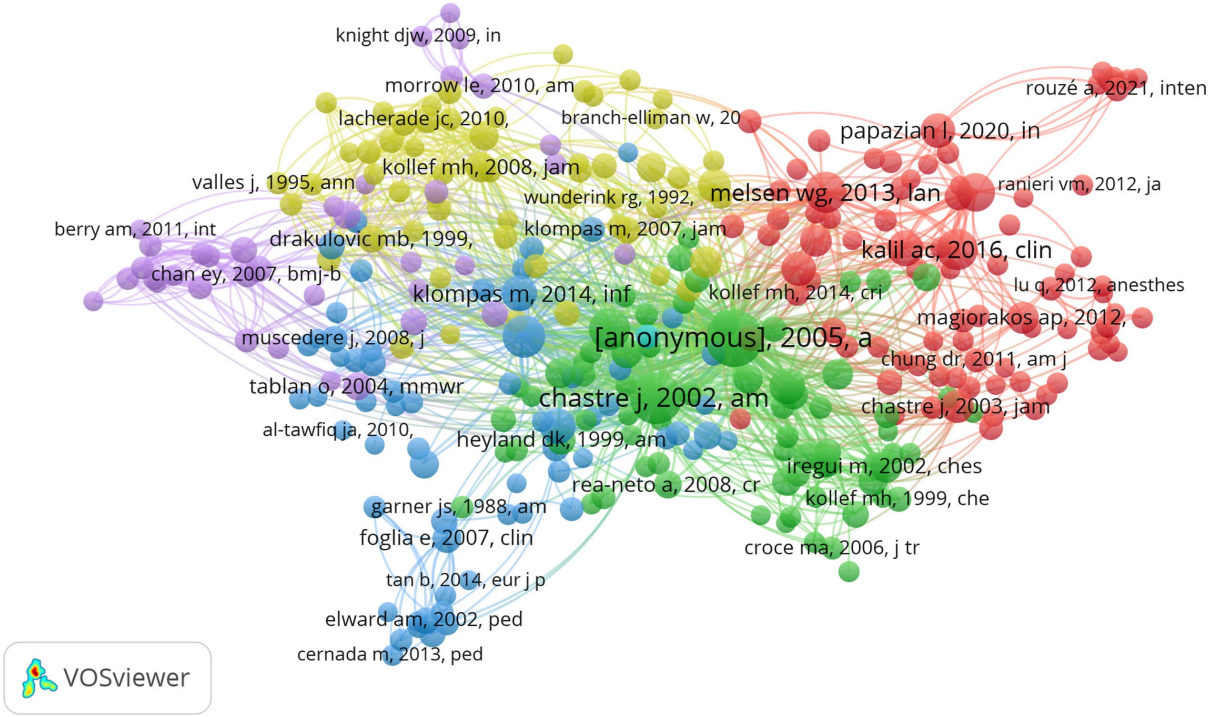
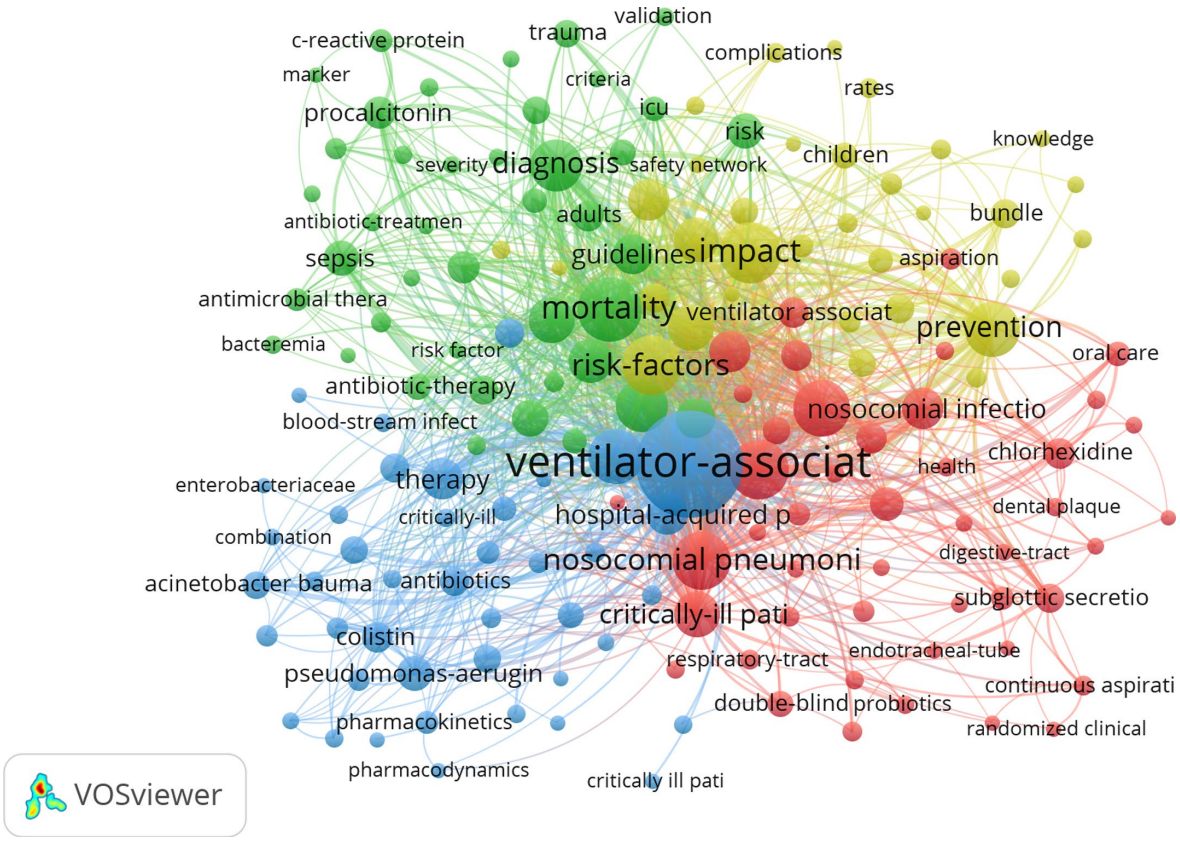


Figure 7. Visualization of the cited literature of ventilator-associated pneumonia research
图 7. VAP 研究共被引文献的可视化

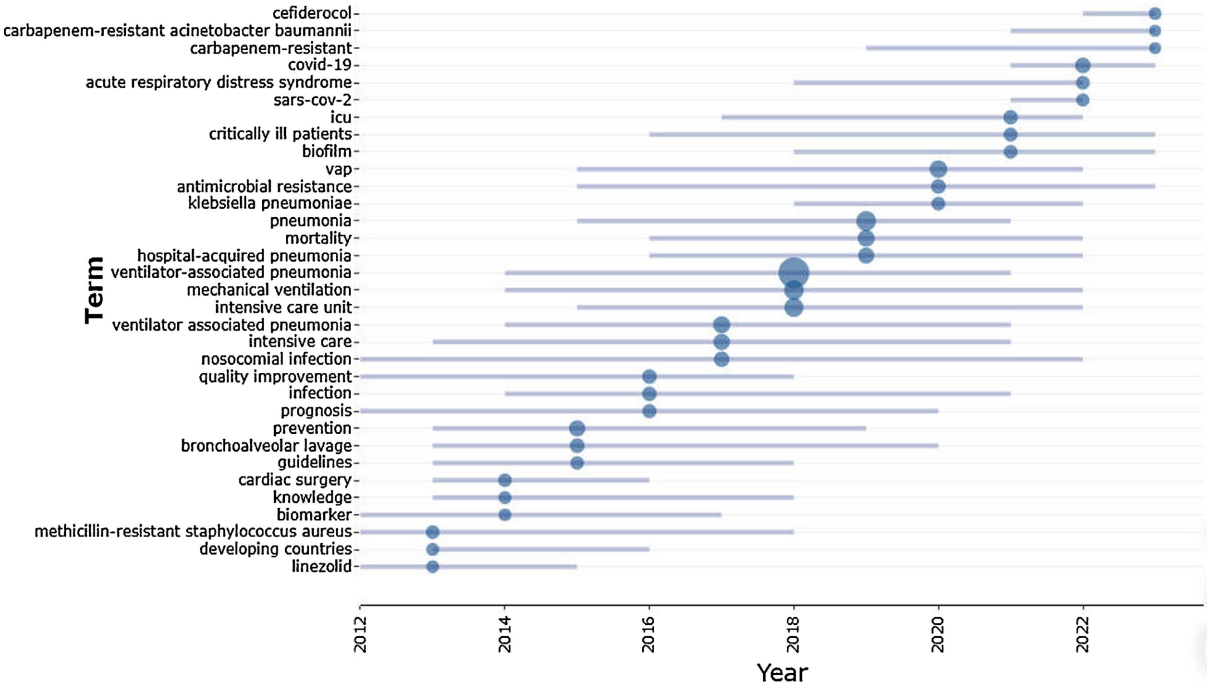
Top 20 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2011 - 2024
Horan TC, 2008, AM J INFECT CONTROL, V36, P309, DOI 10.1016/j.ajic.2008.03.002, DOI	2008	19.68	2011	2013	
Kollef MH, 2008, JAMA-J AM MED ASSOC, V300, P805, DOI 10.1001/jama.300.7.805, DOI	2008	15.78	2011	2013	
Vincent JL, 2009, JAMA-J AM MED ASSOC, V302, P2323, DOI 10.1001/jama.2009.1754, DOI	2009	12.41	2011	2014	
Melsen WG, 2009, CRIT CARE MED, V37, P2709, DOI 10.1097/CCM.0b013e3181ab8655, DOI	2009	10.38	2011	2012	
Bekaert M, 2011, AM J RESP CRIT CARE, V184, P1133, DOI 10.1164/rccm.201105-0867OC, DOI	2011	16.43	2012	2016	
Muscedere J, 2011, CRIT CARE MED, V39, P1985, DOI 10.1097/CCM.0b013e318218a4d9, DOI	2011	13.4	2012	2015	
Labeau SO, 2011, LANCET INFECT DIS, V11, P845, DOI 10.1016/S1473-3099(11)70127-X, DOI	2011	12.2	2012	2015	
Melsen WG, 2013, LANCET INFECT DIS, V13, P665, DOI 10.1016/S1473-3099(13)70081-1, DOI	2013	26.09	2014	2018	
Magiorakos AP, 2012, CLIN MICROBIOL INFEC, V18, P268, DOI 10.1111/j.1469-0691.2011.03570.x, DOI	2012	11.28	2014	2017	
Kalanuria AA, 2014, CRIT CARE, V18, P0, DOI 10.1186/cc13775, DOI	2014	13.5	2015	2019	
Klompas M, 2014, INFECT CONT HOSP EP, V35, P915, DOI 10.1017/S0899823X00193894, DOI	2014	10.66	2016	2019	
Kalil AC, 2016, CLIN INFECT DIS, V63, PE61, DOI 10.1093/cid/ciw353, DOI	2016	41.91	2017	2021	
Kalil AC, 2016, CLIN INFECT DIS, V63, P575, DOI 10.1093/cid/ciw504, DOI	2016	23.14	2017	2021	
Torres A, 2017, EUR RESPIR J, V50, P0, DOI 10.1183/13993003.00582-2017, DOI	2017	35.26	2019	2022	
Koulenti D, 2017, EUR J CLIN MICROBIOL, V36, P1999, DOI 10.1007/s10096-016-2703-z, DOI	2017	14.73	2019	2022	
Papazian L, 2020, INTENS CARE MED, V46, P888, DOI 10.1007/s00134-020-05980-0, DOI	2020	40.65	2021	2024	
Rouzé A, 2021, INTENS CARE MED, V47, P188, DOI 10.1007/s00134-020-06323-9, DOI	2021	14	2021	2024	
Fernando SM, 2020, INTENS CARE MED, V46, P1170, DOI 10.1007/s00134-020-06036-z, DOI	2020	12.08	2021	2024	
Maes M, 2021, CRIT CARE, V25, P0, DOI 10.1186/s13054-021-03460-5, DOI	2021	10.93	2021	2024	
Wu DL, 2019, FRONT PHARMACOL, V10, P0, DOI 10.3389/fphar.2019.00482, DOI	2019	9.79	2021	2024	

Figure 8. Top 20 references with explosive citations
图 8. 引文爆发性强的前 20 位参考文献



(a)



(b)

Figure 9. Ventilator-associated pneumonia research keyword visualization (a) and keyword trend topics (b)
图 9. 关于 VAP 研究的关键词可视化(a)和关键词趋势主题(b)

探讨了新型气管插管及其对 VAP 预防策略的潜在贡献。总体而言，该领域呈上升趋势，越来越多的学者探究 VAP，出现了 Torres A、Rello J 等高生产力的作者。美国是该领域的领先者，出版量最多。中国虽然在出版数量上排名第二，但在前 10 名中没有机构。关键词主要集中在“mechanical ventilation、critical care、mortality、pseudomonas aeruginosa”上，而 cefiderocol、carbapenem-resistant acinetobacter baumannii、COVID-19、acute respiratory distress syndrome 是新兴的研究热点。

4. 研究热点

4.1. Cefiderocol

目前，多重耐药菌引起的感染日益增加，应用合适的抗生素与不良结局直接相关。临床上常见的致病菌包括耐甲氧西林金黄色葡萄球菌、不动杆菌、肺炎克雷伯菌、铜绿假单胞菌等[29]。Cefiderocol (原 S-649266)于 2020 年 9 月获得批准用于治疗呼吸机相关性肺炎[30]。Cefiderocol 是一种新型的头孢菌类抗生素，由头孢菌素部分和儿茶酚型铁载体组成，通过与三价铁结合，并通过细菌铁转运蛋白通过外膜主动转运到细菌细胞中，并通过孔蛋白通道被动扩散到周质间隙[31]，这种方法被称为“特洛伊木马(Trojan horse) [32]”。Cefiderocol 对革兰氏阴性菌具有强活效性，其抗菌活性主要是对 PBP3 的抑制，从而影响细胞壁的合成，导致细胞死亡[33]。临床研究表明，针对有多重耐药感染风险的成人复杂性尿路感染，Cefiderocol 优于亚胺培南－西司他丁[34]。而另外一项随机、双盲、平行组、3 期、非劣效性试验(APEKS-NP)证明，Cefiderocol 单药治疗在由多种革兰氏阴性菌(包括鲍曼不动杆菌、铜绿假单胞菌和肠杆菌属)引起的医院获得性肺炎危重症患者的第 14 天全因死亡率结局方面不劣于高剂量、延长输注美罗培南单药治疗。Cefiderocol 耐受性良好，其安全性与其他头孢菌素类或碳青霉烯类药物一致[35]。一项随机、开放标签、多中心、病原体聚焦、III 期试验中证实碳青霉烯类病原菌感染的患者，使用 Cefiderocol 的临床治疗愈高于最佳治疗组(研究者制定的治疗方案，最多不超过三种药物) [36]。Cefiderocol 主要经肾脏代谢，中重度肾功能损伤的患者在治疗时需要调整剂量[37]。所以，Cefiderocol 可能是治疗 MDR 革兰氏阴性菌感染风险的患者医院获得性肺炎的合适选择[35]。

4.2. 耐碳青霉烯类鲍曼不动杆菌

在重症监护室里，由耐碳青霉烯类鲍曼不动杆菌(CRAB)引起的呼吸机相关肺炎(VAP)是一种严重且具有挑战性的并发症，与不良结果息息相关。目前，CRAB 在世界范围内的流行率不断增长，2017 年，耐碳青霉烯类鲍曼不动杆菌已被世界卫生组织列为危急病原体，治疗选择有限，导致发病率和死亡率不断增加[38]-[40]。在当下，CRAB 引起的感染仍面临许多难题，包括高死亡率、抗生素的选择不当、住院时间延长等。CRAB 的流行与 ICU 内广谱抗生素的过度使用、侵入性操作及医院感染控制措施落实不足密切相关。先前的研究称，与碳青霉烯类敏感的鲍曼不动杆菌患者相比，CRAB 的死亡率是其两倍[41]。CRAB 的耐药机制主要归因于碳青霉烯酶的产生，尤其是碳青霉烯水解 D 类 β-内酰胺酶(CHDL)，包括 OXA-23、-40、-51、-58 [42]和和-143 类 β-内酰胺酶[43]，还包括通过外膜蛋白的改变、外排泵、青霉素结合蛋白的变化[44]。目前临床上针对 CRAB 引起的呼吸机相关性肺炎，抗生素的选择是一大难题，通常粘菌素被认为是首选药物，尽管其有肾毒性和神经毒性[45]。在一项前瞻性研究中，提及大剂量氨苄西林-舒巴坦是治疗鲍曼不动杆菌多重耐药危重患者的安全有效方法[46]。专家认为米诺环素也是治疗 CRAB 感染的合理治疗选择[47]。尽管对于中重度感染的患者，建议联合用药(氨基糖苷类、多粘菌素、替加环素)治疗。而根据试验结果，不建议将粘菌素和美罗培南联合治疗 CRAB 引起的严重感染[48]。与粘菌素单药治疗相比，联合用药是否能改善临床结局仍有待证明。由于抗生素的选择有限，不断寻找更好的治疗方案至关重要。而其他的措施包括集束化管理、医院感染控制也非常重要，加强环境消毒，从

而阻断 CRAB 的传播链条。

4.3. COVID-19 和急性呼吸窘迫综合征

2019 年底，新型冠状病毒(SARS-CoV-2)在全球范围内流行，患者出现呼吸窘迫从而入住重症监护室，其中高达 80%的患者要进行有创通气[49]。机械通气、体位、患者基础疾病、神经肌肉阻滞剂、免疫抑制状态等因素均可导致 VAP 的发生。有报告证明，COVID 的患者发生呼吸机相关性肺炎的概率较高[50] [51]。这可能与长时间的有创机械通气、俯卧位治疗、接受更多的免疫抑制药物治疗、使用 ECMO 有关[52]。除此之外，COVID-19 导致的严重淋巴细胞减少症也增加了继发感染的风险[53]。免疫系统在 COVID-19 中发挥着双重作用，一方面有利于促炎细胞因子的消退，另一方面促进 ARDS 的发展[54]。COVID-19 引起的急性呼吸窘迫综合征(ARDS)患者是发生 VAP 的高危人群，相比于无 ARDS 的患者，其发生率可能高达 60%，继而出现全身炎症反应综合征、器官损伤，同时伴随免疫抑制[55]-[57]。先前已有明确证据表明，免疫细胞功能障碍相关的三种细胞表面标志物(T 细胞、单核细胞和中性粒细胞)可以预测感染的危险分层[58] [59]。有研究发现其中中性粒细胞功能受损的关键是补体 C5a 的诱导[60] [61]。而 COVID-19 患者的免疫功能明显抑制，从而炎症因子激活和器官损伤以及抗菌功能失调，引起补体 C5a 的激活进一步有助于炎症因子的释放[62]。COVID-19 引起的细胞因子风暴导致血管通透性增加，继而引发 ARDS [63]。目前，关于发生 VAP 的 ARDS 患者相关死亡率的研究较少，大多数研究集中在使用肺保护性机械通气策略之前进行的。先前研究报道，在严重 ARDS 患者中，根据标准化肺保护策略进行通气，VAP 的发生与 ICU 死亡风险较高相关[64]。COVID-19、ARDS 和 VAP 的关联本质上是“病原侵袭–过度炎症–医源性损伤”的连续病理过程。COVID-19 通过诱发 ARDS 为 VAP 创造条件，而 VAP 进一步加剧肺损伤，延长机械通气时间，显著增加患者死亡风险。临床中，早期识别 COVID-19 重症倾向，阻断 ARDS 进展，一旦启动机械通气，即启动 VAP 的预防策略。

5. 优势与不足

本文利用文献计量学的方式分析呼吸机相关性肺炎的研究现状，通过软件程序探讨了研究热点和前沿，有助于我们更好地了解呼吸机相关性肺炎。但是，本研究仍存在一些局限性。我们只检索了 Web of Science 中收录的英文文献。因此，数据可能不够全面。以其他语言和数据库发表的文章需要进一步研究。此外，在我们的文献计量分析中应用的软件在整合来自不同资源的数据方面存在困难。一些没有引用的出版物不一定没有科学价值。尽管如此，使用可视化方法来了解一个领域的当前状态、热点和趋势仍然是有价值的。

在过去十多年里，美国是 VAP 研究的领先国家。使用 CiteSpace 和 VOSviewer 软件的视觉分析显示了 VAP 的研究现状。在国际核心期刊上发表的文章越来越多，不同国家的专家和机构之间的合作和沟通不断加强。当下，呼吸机相关性肺炎的诊断尚未形成共识，所以这仍是一个挑战。cefiderocol、carbapenem-resistant acinetobacter baumannii、COVID-19、acute respiratory distress syndrome 仍将是未来研究的重点，特别是多重耐药菌引起的呼吸机相关性肺炎，抗生素的应用至关重要。不断开发新型抗菌药物和完善治疗策略是当前重中之重。

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