Review

Current Challenges and Future Directions in the Management of Inflammatory Breast Cancer: A Review

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Abstract: (1) Background: Inflammatory breast cancer (IBC) is a rare and aggressive form of breast cancer that poses unique management challenges. This review aims to synthesize the current literature on IBC, focusing on diagnosis, treatment, and prognosis, while highlighting recent advances and ongoing issues in patient management.; (2) Methods: We outline the typical clinical presentation and diagnostic criteria of IBC. Additionally, we detail the main therapeutic strategies, including neoadjuvant chemotherapy, surgery, radiation therapy, targeted therapies, hormonal therapies, and emerging treatments such as immunotherapy. The review is based on a comprehensive analysis of the existing literature.; (3) Results: Despite advancements in systemic therapy and a better understanding of IBC biology, the prognosis for patients with IBC remains poor. The overall survival rate has shown only marginal improvement over the past few decades. Future research directions, including the identification of novel biomarkers for early detection and personalized medicine strategies, are identified. The need for more high-quality clinical trials to address the challenges in IBC management is emphasized.; (4) Conclusions: Managing IBC is a complex task that necessitates multidisciplinary care and patient-centered communication. This review provides clinicians and researchers with a comprehensive overview of the current challenges and future directions in IBC management. The goal is to guide treatment decisions and inform further research, ultimately improving patient outcomes and prognosis.

Keywords: inflammatory breast cancer (IBC); review; immunotherapy; targeted therapy; tumor microenvironment

1. Introduction

1.1. Clinical and Diagnostic Characteristics of Inflammatory Breast Cancer (IBC):

Clinical and Diagnostic Characteristics of Inflammatory Breast Cancer (IBC): IBC is characterized by a unique and aggressive pathology, displaying symptoms such as erythema (redness), edema (swelling), and peau d'orange (skin resembling an orange peel).[1,2] These symptoms are generally diffused rather than localized, involving a significant portion of the breast. Furthermore, the disease often manifests with a palpable boundary and rapidly progresses to an advanced stage.[2]

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From a pathological perspective, IBC is frequently associated with dermal lymphovascular tumor emboli, observable via biopsy and considered one of the disease's defining features. More aggressive triple-negative and HER2-positive breast cancer subtypes are significantly represented in IBC compared to non-IBC, leading to poorer prognoses in response to conventional therapies.[3]

The process of diagnosing IBC has traditionally been subjective, largely reliant on clinical observation and patient reports.[4] However, this approach's shortcomings have prompted the development of a more formal, objective definition of IBC. An expert panel, including representatives from Susan G. Komen, the Inflammatory Breast Cancer Research Foundation, and the Milburn Foundation, proposed a novel quantitative scoring system. This diagnostic approach, providing a continuous score from 0 to 48, incorporates clinical, pathological, and imaging features with the aim to increase diagnostic accuracy and influence treatment decisions and clinical trial inclusion. The proposed system, however, is yet to be validated in extensive studies.[2]

The distinct clinical and diagnostic characteristics of IBC emphasize the challenge of managing this aggressive disease and underscore the necessity for improved diagnostic tools and therapeutic strategies rooted in extensive scientific research and clinical trials.[5]

1.2. Current Treatments for IBC:

IBC is traditionally treated with the 'Trimodality Treatment' method, comprising systemic treatment, surgery, and radiation.[6] The systemic therapy often borrows data from non-IBC clinical trials due to the disease's rarity, raising questions about the applicability of such data to IBC. However, these therapeutic strategies have evolved over the years, incorporating targeted therapies in combination with chemotherapy.[7]

Clinical trials play a critical role in understanding the varying effects of these therapies on pathologic complete response (pCR) and survival outcomes. They also help identify predictive markers and understand adverse events associated with these therapies.[8]

Promising advancements in IBC treatment include immunotherapy, which leverages the body's immune system to fight cancer cells, and the introduction of immune checkpoint inhibitors. The latter block the signals that allow cancer cells to evade the immune system, marking a significant milestone in cancer treatment.[9]

Additionally, targeted therapies such as CDK4/6 inhibitors and anti-HER2 therapies have shown effectiveness in managing IBC.[10] CDK4/6 inhibitors halt proteins that stimulate cell division, thereby slowing or stopping cancer cell proliferation.[11] Anti-HER2 therapies target the HER2 protein, which is overexpressed in certain types of breast cancer, including a substantial number of IBC cases.[12]

Despite these advancements, the current therapeutic landscape for IBC presents challenges. The diversity and aggressive nature of IBC necessitate a more personalized treatment approach.[13] Hence, the development of novel systemic treatments and IBC-specific clinical trials is essential.[14] Data from these trials could inform innovative treatment strategies, clarify uncertainties in real-world practice, and potentially revolutionize IBC clinical management.[15] Moreover, genomic technologies, gene-expression profiling of tumor tissue, and liquid biopsy techniques could guide treatment decisions and provide insights into the molecular drivers of the disease.[16]

While the current treatments have significantly improved some patients' prognosis, they do not offer a universally effective solution.[17] Thus, there is an urgent need for additional research into both the treatment approaches and the underlying biology of IBC.[18] Guided by robust clinical trial results, the ultimate aim is to improve treatment response, prolong survival for metastatic patients, achieve superior local control, and potentially increase the cure rate for locally advanced disease.[19]

2. Materials and Methods

To provide a comprehensive understanding of the current landscape of Inflammatory Breast Cancer (IBC) treatment, this review was orchestrated using a rigorous and methodical search strategy.[20] The main objective was to identify and synthesize all pertinent studies related to the

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management of IBC, while critically discussing the challenges faced and prospective future directions.

The search strategy was divided into three stages for systematic data collection and review. Firstly, a comprehensive search was conducted across three major electronic databases: PubMed, Google Scholar, Embase, MEDLINE, Web of Science.[21] To capture a broad range of relevant studies, the search employed a combination of keywords, including "Inflammatory Breast Cancer," "therapy," and "biomarkers". Recognizing the global reach of research, the search was limited to articles published in English but did not limit any specific date range. This open time frame permitted us to acknowledge significant historical contributions to the field and to ensure a robust understanding of the disease's progression.

The types of articles considered for inclusion in the review were broad, encompassing both original research articles and reviews. This approach was adopted to gain a comprehensive understanding of the topic from both primary data and interpretive analyses.[22]

The second stage involved the meticulous selection of relevant studies. An initial screening of the article titles and abstracts was performed to evaluate their relevance to the topic at hand. Subsequently, full-text articles were reviewed thoroughly to determine their eligibility based on pre-set criteria. The criteria for inclusion in the review were stringent, focusing on the study's primary emphasis on IBC treatment, its discussion of current challenges, and its proposal for future research directions in the field. Conversely, studies were excluded if they were tangentially related to IBC, lacked sufficient detail, were not available in full text, or did not contribute substantially to the understanding of IBC management. In addition, we performed a manual review of the references cited in the selected studies to identify additional pertinent articles that might have been overlooked during the database search.[23]

The third and final stage of the methodology was data extraction. A diligent and comprehensive extraction of information was performed on the eligible studies. The data extracted included the study characteristics (e.g., first author, year of publication, study design), the clinical and diagnostic characteristics of IBC presented, the current treatments discussed, the challenges identified in the treatment of IBC, and the suggested future directions in the field.[24]

This methodical approach facilitated a comprehensive and objective synthesis of the existing literature relating to the diagnosis, treatment, and future research directions in IBC management. It allowed us to not only understand the current state of the field but also identify knowledge gaps that future research needs to address. Ultimately, this comprehensive review methodology aimed to create a resource that would enable a better understanding of IBC and guide future studies to improve the disease's diagnosis and treatment.

3. Results

The diagnosis and treatment of Inflammatory Breast Cancer (IBC) present a complex challenge due to several factors. These include the disease's aggressive behavior, resistance to conventional chemotherapy, propensity for angiogenesis, high metastatic potential, and a distinct but poorly understood biology. These characteristics culminate in less effective outcomes when treated with the current standard-of-care modalities.[25]

One of the significant obstacles in the effective management of IBC is the absence of a precise, objective definition for the disease. This gap has led to a patient population that is quite heterogenous, thereby complicating the clinical care, the design and execution of clinical trials, and the quest for IBC-specific biomarkers and treatments.[2,26]

Delving deeper into the intricacies of the disease, it becomes evident that the tumor microenvironment (TME) in IBC, encompassing inflammatory and immune cells, blood vessels, and the extracellular matrix, is pivotal to the disease's pathogenesis and aggressive behavior.[27,28] The elaborate interplay between the intrinsic and extrinsic components of IBC, orchestrated by a myriad of cytokines and chemokines, significantly contributes to the tumor's robust aggressiveness and angiogenic potential.[29]

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In addition, despite IBC having a unique clinical presentation that distinguishes it from non-IBC forms, the precise molecular mechanisms underpinning the disease remain elusive.[30] Treatments that have proven successful in non-IBC, such as targeted therapies for HER2 positive and hormonal receptor positive non-IBC, have resulted in improved patient outcomes.[25,31] However, applying these treatment strategies to IBC poses a considerable challenge, attributable to the unique biology of the disease.

Furthermore, while the role of systemic treatments for IBC, including chemotherapy, targeted therapies, and immunotherapy, has evolved significantly over time, the rarity of the disease implies that these therapies often derive from non-IBC clinical trials. This factor presents yet another significant hurdle in optimizing treatment for IBC patients.[25] There is a pressing need for IBC-specific clinical trials, which would potentially lead to more tailored and effective treatment strategies for this aggressive cancer type. The future direction, therefore, necessitates the formulation of novel systemic treatments, with a particular focus on IBC-specific clinical trials.[32]

To advance in the battle against IBC, a more profound understanding of the tumor biology is required, particularly with respect to the tumor microenvironment and the intricate interplay between various molecular and cellular components. This understanding is crucial in refining our definition of IBC as a unique entity within breast cancer, thereby facilitating the development of IBC-specific diagnostic and treatment strategies.[33]

Finally, there is a need to explore novel immunotherapeutic approaches for IBC, especially immune checkpoint inhibitors, CDK4/6 inhibitors, and anti-HER2 therapy.[14] The ultimate objective transcends enhancing the pathological response rate to eradicating distant metastases, which are the primary cause of patient death.[34] Given IBC's aggressive nature and poor prognosis, there is an urgent and compelling need to address these challenges. The aim is to redirect future research towards improving treatment outcomes for IBC patients, which will ultimately transform patient care for this rare and aggressive form of breast cancer.[34,35]

4. Discussion

The management of inflammatory breast cancer (IBC) persists as a critical issue in the broader field of oncology, despite numerous breakthroughs in other areas. This comprehensive review investigates our existing knowledge and therapeutic methodologies, thereby underscoring the necessity for rigorous research aimed at improving the outcomes for patients suffering from IBC.

IBC's unique clinical presentation, which sets it apart from other forms of breast cancer, is unfortunately often determined by subjective diagnoses.[36] This practice has led to a heterogeneous patient population. The absence of a precise and universally accepted definition for IBC poses substantial difficulties in the design and execution of clinical trials. Consequently, the development of specifically tailored therapies and biomarkers for IBC is often delayed.[37] However, current initiatives aimed at developing a more standardized and objective diagnostic system for IBC offer hope. The proposed system would not only enhance diagnostic precision but also provide further insights into the complex pathobiology of IBC.

Therapeutically, IBC has traditionally been managed using the 'Trimodality Treatment' approach. This regimen combines systemic therapy, surgical procedures, and radiation therapy.[38] Nevertheless, these methodologies are typically extrapolated from non-IBC clinical trials due to the scarcity of IBC-specific studies. Despite the significant promise shown by recent advancements in immunotherapy and targeted therapies, their effectiveness varies widely. This variation highlights the necessity for conducting clinical trials specifically designed for IBC.[39]

The tumor microenvironment in IBC significantly contributes to the disease's aggressive nature and resistance to conventional treatment modalities.[40,41] The intricate interplay between intrinsic and extrinsic factors within the tumors. This complex interaction, mediated by various cytokines and chemokines, lends to its high angiogenic potential. IBC tumor cells resemble non-IBC cells, but often demonstrate distinct features like dermal lymphatic invasion. The understanding of its genetic profile, including tumor markers like ZEB1, E-cadherin, ALDH1, NOTCH3, and genetic alterations such as MYC, PIK3CA, HER2, FGFR1, p53, BRCA2, and PTEN, could facilitate the development of

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targeted therapies and ultimately improve patient prognosis. [41] Therefore, gaining a more profound understanding of this tumor microenvironment could potentially facilitate the development of innovative therapeutic strategies.

Developments in genomic technologies and the discovery of new biomarkers could potentially lead to the implementation of personalized medicine strategies, which may improve treatment outcomes.[42] Furthermore, Incorporating novel systemic treatments, including innovative immunotherapeutic approaches, offers substantial potential for enhancing the prognosis of patients diagnosed with Inflammatory Breast Cancer (IBC). The targeted therapies like Trastuzumab, Pertuzumab, Lapatinib, Trastuzumab emtansine, Neratinib, Bevacizumab, Panitumumab, and Pazopanib are making strides in IBC treatment, particularly when considering the individualized cancer subtypes.[25] The future of IBC treatment could potentially see a shift from high-toxicity chemotherapies to these more tailored and effective treatments, enhancing patient prognosis and quality of life. An increased emphasis on conducting IBC-specific clinical trials could significantly enhance the effectiveness of tailored treatment strategies for this aggressive disease.

However, realizing these potential improvements requires concerted and high-quality research efforts specifically focused on IBC. Global collaborations will be necessary to secure funding and conduct essential basic science and clinical research. Participation from multidisciplinary teams composed of clinicians, researchers, patients, and advocacy groups is crucial for these efforts. The results obtained from such collaborations will be instrumental in supporting the conclusions drawn and guiding the future direction of IBC management strategies.

5. Conclusions

This comprehensive and rigorous review of the present landscape of Inflammatory Breast Cancer (IBC) management reiterates the essential requirement for a more accurate, objective definition of the disease. The creation of such a definition serves as a solid cornerstone for the design and execution of effective clinical trials, aiding the accelerated development of IBC-specific therapies and biomarkers. Our in-depth exploration of the available literature accentuates the pivotal role that the tumor microenvironment plays in IBC's notorious aggressiveness and its resistance to existing treatment modalities. This understanding strongly implies that delving deeper into these complex interactions and dynamics could be the key to unlocking innovative and potentially more effective therapeutic approaches.

Despite the numerous challenges currently marring the understanding and management of IBC, this review has unearthed several promising avenues for the future. The dawn of genomic technologies and the consistent discovery of new biomarkers are catapulting us into a new era in the field of oncology, one that is marked by the promise of personalized medicine strategies. Such strategies would be tailored to cater to individual patient characteristics and needs, thereby enhancing treatment outcomes. Concurrently, the potential emergence of novel systemic treatments and the urgent call for IBC-specific clinical trials bode well for significant improvements in patient outcomes.

However, realizing these promising advancements necessitates the conduct of robust, high-quality research, employing advanced methodologies with an unwavering commitment to precision and accuracy. Achieving this ambitious objective requires a global, cross-disciplinary collaborative effort. This effort should bring together the skills, knowledge, and resources of clinicians, researchers, patients, and advocacy groups from across the world, united in their determination to tackle the challenges posed by IBC.

The complexities of IBC management demand persistent, innovative research, and resolute collaboration. Through our collective endeavors, we can hope to confront and overcome the clinical challenges currently presented by IBC. Our dedication has the potential to significantly improve survival rates and enhance the quality of life for patients grappling with this aggressive form of breast cancer. The battle against IBC is undoubtedly a difficult one, but with our continued commitment, worldwide collaboration, and scientific advancements, we are better equipped than ever to take on these challenges and strive towards a future where IBC is effectively managed.

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References

1. Menta A, Fouad TM, Lucci A, Le-Petross H, Stauder MC, Woodward WA, Ueno NT, Lim B. Inflammatory Breast Cancer: What to Know About This Unique, Aggressive Breast Cancer. Surg Clin N. Am. 2018 Aug;98(4):787-800. doi:10.1016/j.suc.2018.03.009. Epub 2018 May 24. PMID: 30005774.
2. Jagsi R, Mason G, Overmoyer BA, Woodward WA, Badve S, Schneider RJ, Lang JE, Alpaugh M, Williams KP, Vaught D, Smith A, Smith K, Miller KD; Susan G. Komen-IBCRF IBC Collaborative in partnership with the Milburn Foundation. Inflammatory breast cancer defined: proposed common diagnostic criteria to guide treatment and research. Breast Cancer Res Treat. 2022 Apr;192(2):235-243. doi: 10.1007/s10549-021-06434-x. Epub 2022 Jan 1. Erratum in: Breast Cancer Res Treat. 2022 Feb 8; PMID: 34973083; PMCID: PMC8926970.
3. Di Bonito M, Cantile M, Botti G. Pathological and molecular characteristics of inflammatory breast cancer. Transl Cancer Res. 2019 Oct;8(Suppl 5):S449-S456. doi: 10.21037/tcr.2019.03.24. PMID: 35117122; PMCID: PMC8798351.
4. Schairer C, Hablas A, Eldein IAS, Gaafar R, Rais H, Mezlini A, Ayed FB, Ayoub WB, Benider A, Tahri A, Khouchani M, Aboulazm D, Karkouri M, Eissa S, Pfeiffer RM, Gadalla SM, Swain SM, Merajver SD, Brown LM, Soliman AS. Clinico-pathologic and mammographic characteristics of inflammatory and non-inflammatory breast cancer at six centers in North Africa. Breast Cancer Res Treat. 2019 Jul;176(2):407-417. doi: 10.1007/s10549-019-05237-5. Epub 2019 Apr 22. PMID: 31006821; PMCID: PMC6705400.
5. Koch RM, Principe DR, Cataneo JL, Rana A. Progress for Immunotherapy in Inflammatory Breast Cancer and Emerging Barriers to Therapeutic Efficacy. Cancers (Basel). 2021 May 22;13(11):2543. doi: 10.3390/cancers13112543. PMID: 34067257; PMCID: PMC8196819.
6. Relation T, Li Y, Fisher JL, Tsung A, Oppong B, Eskander MF, Obeng-Gyasi S. Inflammatory breast cancer, trimodal treatment, and mortality: Does where you live matter? Surgery. 2022 Mar;171(3):687-692. doi: 10.1016/j.surg.2021.08.061. Epub 2021 Nov 30. PMID: 34857388; PMCID: PMC8885962.
7. Zhang BN, Cao XC, Chen JY, Chen J, Fu L, Hu XC, Jiang ZF, Li HY, Liao N, Liu DG, Tao O, Shao ZM, Sun Q, Wang S, Wang YS, Xu BH, Zhang J. Guidelines on the diagnosis and treatment of breast cancer (2011 edition). Gland Surg. 2012 May;1(1):39-61. doi: 10.3978/j.issn.2227-684X.2012.04.07. PMID: 25083426; PMCID: PMC4115707.
8. Biswas T, Jindal C, Fitzgerald TL, Efird JT. Pathologic Complete Response (pCR) and Survival of Women with Inflammatory Breast Cancer (IBC): An Analysis Based on Biologic Subtypes and Demographic Characteristics. Int J Environ Res Public Health. 2019 Jan 4;16(1):124. doi: 10.3390/ijerph16010124. PMID: 30621221; PMCID: PMC6339010.
9. Dawood S, Cristofanilli M. IBC as a Rapidly Spreading Systemic Disease: Clinical and Targeted Approaches Using the Neoadjuvant Model. J Natl Cancer Inst Monogr. 2015 May;2015(51):56-9. doi: 10.1093/jncimonographs/lgv017. PMID: 26063888.
10. Sobhani N, D'Angelo A, Pittacolo M, Roviello G, Miccoli A, Corona SP, Bernocchi O, Generali D, Otto T. Updates on the CDK4/6 Inhibitory Strategy and Combinations in Breast Cancer. Cells. 2019 Apr 6;8(4):321. doi: 10.3390/cells8040321. PMID: 30959874; PMCID: PMC6523967.
11. Pernas S, Tolaney SM, Winer EP, Goel S. CDK4/6 inhibition in breast cancer: current practice and future directions. Ther Adv Med Oncol. 2018 Jul 17;10:1758835918786451. doi: 10.1177/1758835918786451. PMID: 30038670; PMCID: PMC6050811.
12. Oh DY, Bang YJ. HER2-targeted therapies - a role beyond breast cancer. Nat Rev Clin Oncol. 2020 Jan;17(1):33-48. doi: 10.1038/s41571-019-0268-3. Epub 2019 Sep 23. PMID: 31548601.

13. Vafaizadeh V, Barekati Z. Immuno-Oncology Biomarkers for Personalized Immunotherapy in Breast Cancer. Front Cell Dev Biol. 2020 Mar 17;8:162. doi: 10.3389/fcell.2020.00162. PMID: 32258038; PMCID: PMC7089925.
14. Chainitikun S, Mingmalairak S, Parinyanitikul N. What is the best systemic treatment for newly diagnosed inflammatory breast cancer?-a narrative review. Chin Clin Oncol. 2021 Dec;10(6):55. doi: 10.21037/cco-21-81. Epub 2021 Oct 19. PMID: 34670376.
15. Vagia E, Cristofanilli M. New Treatment Strategies for the Inflammatory Breast Cancer. Curr Treat Options Oncol. 2021 Apr 24;22(6):50. doi: 10.1007/s11864-021-00843-2. PMID: 33893888.
16. Kertmen N, Babacan T, Keskin O, Solak M, Sarici F, Akin S, Arik Z, Aslan A, Ates O, Aksoy S, Ozisik Y, Altundag K. Molecular subtypes in patients with inflammatory breast cancer; a single center experience. J BUON. 2015 Jan-Feb;20(1):35-9. PMID: 25778293.
17. Korde LA, Somerfield MR, Carey LA, Crews JR, Denduluri N, Hwang ES, Khan SA, Loibl S, Morris EA, Perez A, Regan MM, Spears PA, Sudheendra PK, Symmans WF, Yung RL, Harvey BE, Hershman DL. Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline. J Clin Oncol. 2021 May 1;39(13):1485-1505. doi: 10.1200/JCO.20.03399. Epub 2021 Jan 28. PMID: 33507815; PMCID: PMC8274745.
18. Bayraktar S, Batoo S, Okuno S, Glück S. Immunotherapy in breast cancer. J Carcinog. 2019 May 23;18:2. doi: 10.4103/jcar.JCar_2_19. PMID: 31160888; PMCID: PMC6540776.
19. Cardoso F, Senkus E, Costa A, Papadopoulos E, Aapro M, André F, Harbeck N, Aguilar Lopez B, Barrios CH, Bergh J, Biganzoli L, Boers-Doets CB, Cardoso MJ, Carey LA, Cortés J, Curigliano G, Diéras V, El Saghir NS, Eniu A, Fallowfield L, Francis PA, Gelmon K, Johnston SRD, Kaufman B, Koppikar S, Krop IE, Mayer M, Nakigudde G, Offersen BV, Ohno S, Pagani O, Paluch-Shimon S, Penault-Llorca F, Prat A, Rugo HS, Sledge GW, Spence D, Thomssen C, Vorobiof DA, Xu B, Norton L, Winer EP. 4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4)†. Ann Oncol. 2018 Aug 1;29(8):1634-1657. doi: 10.1093/annonc/mdy192. PMID: 30032243; PMCID: PMC7360146.
20. Hopp L, Rittenmeyer L. Review and Synthesize Completed Research Through Systematic Review. West J Nurs Res. 2015 Oct;37(10):1359-72. doi: 10.1177/0193945915578540. Epub 2015 Apr 6. PMID: 25845805.
21. Bramer WM, Rethlefsen ML, Kleijnen J, Franco OH. Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. Syst Rev. 2017 Dec 6;6(1):245. doi: 10.1186/s13643-017-0644-y. PMID: 29208034; PMCID: PMC5718002.
22. Paré G, Kitsiou S. Chapter 9 Methods for Literature Reviews. In: Lau F, Kuziemsky C, editors. Handbook of eHealth Evaluation: An Evidence-based Approach [Internet]. Victoria (BC): University of Victoria; 2017 Feb 27.
23. Sriganesh K, Shanthanna H, Busse JW. A brief overview of systematic reviews and meta-analyses. Indian J Anaesth. 2016 Sep;60(9):689-694. doi: 10.4103/0019-5049.190628. PMID: 27729699; PMCID: PMC5037953.
24. Jonnalagadda SR, Goyal P, Huffman MD. Automating data extraction in systematic reviews: a systematic review. Syst Rev. 2015 Jun 15;4:78. doi: 10.1186/s13643-015-0066-7. PMID: 26073888; PMCID: PMC4514954.
25. Chainitikun S, Saleem S, Lim B, Valero V, Ueno NT. Update on systemic treatment for newly diagnosed inflammatory breast cancer. J Adv Res. 2020 Aug 29;29:1-12. doi: 10.1016/j.jare.2020.08.014. PMID: 33842000; PMCID: PMC8020152.
26. Menta A, Fouad TM, Lucci A, Le-Petross H, Stauder MC, Woodward WA, Ueno NT, Lim B. Inflammatory Breast Cancer: What to Know About This Unique, Aggressive Breast Cancer. Surg Clin North Am. 2018 Aug;98(4):787-800. doi: 10.1016/j.suc.2018.03.009. Epub 2018 May 24. PMID: 30005774.
27. Huang A, Cao S, Tang L. The tumor microenvironment and inflammatory breast cancer. J Cancer. 2017 Jul 3;8(10):1884-1891. doi: 10.7150/jca.17595. PMID: 28819386; PMCID: PMC5556652.
28. Koch RM, Principe DR, Cataneo JL, Rana A. Progress for Immunotherapy in Inflammatory Breast Cancer and Emerging Barriers to Therapeutic Efficacy. Cancers (Basel). 2021 May 22;13(11):2543. doi: 10.3390/cancers13112543. PMID: 34067257; PMCID: PMC8196819.
29. Morrow RJ, Etemadi N, Yeo B, Ernst M. Challenging a Misnomer? The Role of Inflammatory Pathways in Inflammatory Breast Cancer. Mediators Inflamm. 2017;2017:4754827. doi: 10.1155/2017/4754827. Epub 2017 May 14. PMID: 28607534; PMCID: PMC5457777.
30. Balema W, Liu D, Shen Y, El-Zein R, Debeb BG, Kai M, Overmoyer B, Miller KD, Le- Petross HT, Ueno NT, Woodward WA. Inflammatory breast cancer appearance at presentation is associated with overall survival.

Cancer Med. 2021 Sep;10(18):6261- 6272. doi: 10.1002/cam4.4170. Epub 2021 Jul 30. PMID: 34327874; PMCID: PMC8446552.

31. Chainitikun S, Espinosa Fernandez JR, Long JP, Iwase T, Kida K, Wang X, Saleem S, Lim B, Valero V, Ueno NT. Pathological complete response of adding targeted therapy to neoadjuvant chemotherapy for inflammatory breast cancer: A systematic review. PLoS One. 2021 Apr 16;16(4):e0250057. doi: 10.1371/journal.pone.0250057. PMID: 33861773; PMCID: PMC8051801.
32. Newman AB, Lynce F. Tailoring Treatment for Patients with Inflammatory Breast Cancer. Curr Treat Options Oncol. 2023 Jun;24(6):580-593. doi: 10.1007/s11864-023-01077-0. Epub 2023 Apr 12. PMID: 37043118.
33. Lim B, Woodward WA, Wang X, Reuben JM, Ueno NT. Inflammatory breast cancer biology: the tumour microenvironment is key. Nat Rev Cancer. 2018 Aug;18(8):485-499. doi: 10.1038/s41568-018-0010-y. Erratum in: Nat Rev Cancer. 2018 May 10;: PMID: 29703913.
34. Dano D, Lardy-Cleaud A, Monneur A, Quenel-Tueux N, Levy C, Mouret-Reynier MA, Coudert B, Mailliez A, Ferrero JM, Guiu S, Campone M, de La Motte Rouge T, Petit T, Pistilli B, Dalenc F, Simon G, Lerebours F, Chabaud S, Bertucci F, Gonçalves A. Metastatic inflammatory breast cancer: survival outcomes and prognostic factors in the national, multicentric, and real-life French cohort (ESME). ESMO Open. 2021 Aug;6(4):100220. doi: 10.1016/j.esmoop.2021.100220. Epub 2021 Jul 22. PMID: 34303929; PMCID: PMC8327489.
35. Weiss A, Menen RS, Lin HY, Shen Y, Rosso KJ, Shaitelman S, Woodward W, Valero V, Ueno NT, Bedrosian I, Babiera G. Factors associated with improved outcomes for metastatic inflammatory breast cancer patients. Breast Cancer Res Treat. 2018 Jun;169(3):615-623. doi: 10.1007/s10549-018-4715-0. Epub 2018 Feb 19. PMID: 29460033.
36. Chippa V, Barazi H. Inflammatory Breast Cancer. 2023 Apr 16. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 33231994.
37. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, Ji X, Liu W, Huang B, Luo W, Liu B, Lei Y, Du S, Vuppalapati A, Luu HH, Haydon RC, He TC, Ren G. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. Genes Dis. 2018 May 12;5(2):77- 106. doi: 10.1016/j.gendis.2018.05.001. PMID: 30258937; PMCID: PMC6147049.
38. Relation T, Li Y, Fisher JL, Tsung A, Oppong B, Eskander MF, Obeng-Gyasi S. Inflammatory breast cancer, trimodal treatment, and mortality: Does where you live matter? Surgery. 2022 Mar;171(3):687-692. doi: 10.1016/j.surg.2021.08.061. Epub 2021 Nov 30. PMID: 34857388; PMCID: PMC8885962.
39. Koch RM, Principe DR, Cataneo JL, Rana A. Progress for Immunotherapy in Inflammatory Breast Cancer and Emerging Barriers to Therapeutic Efficacy. Cancers (Basel). 2021 May 22;13(11):2543. doi: 10.3390/cancers13112543. PMID: 34067257; PMCID: PMC8196819.
40. Son B, Lee S, Youn H, Kim E, Kim W, Youn B. The role of tumor microenvironment in therapeutic resistance. Oncotarget. 2017 Jan 17;8(3):3933-3945. doi: 10.18632/oncotarget.13907. PMID: 27965469; PMCID: PMC5354804.
41. Dobiasova B, Mego M. Biomarkers for Inflammatory Breast Cancer: Diagnostic and Therapeutic Utility. Breast Cancer (Dove Med Press). 2020 Oct 14;12:153-163. doi: 10.2147/BCTT.S231502. PMID: 33116817; PMCID: PMC7569067.
42. Ho D, Quake SR, McCabe ERB, Chng WJ, Chow EK, Ding X, Gelb BD, Ginsburg GS, Hassenstab J, Ho CM, Mobley WC, Nolan GP, Rosen ST, Tan P, Yen Y, Zarrinpar A. Enabling Technologies for Personalized and Precision Medicine. Trends Biotechnol. 2020 May;38(5):497-518. doi: 10.1016/j.tibtech.2019.12.021. Epub 2020 Jan 21. PMID: 31980301; PMCID: PMC7924935.