

Global Research Trends and Future Direction in Peripartum Cardiomyopathy: A Bibliometric Analysis

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doi: 10.5455/aim.2023.31.270-274

ACTA INFORM MED. 2023, 31(4): 270-274

Received: NOV 15, 2023

Accepted: DEC 17, 2023

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ABSTRACT

Background: Peripartum cardiomyopathy (PPCM) is a pregnancy-related myocardial disease. PPCM has a high morbidity and mortality rate, but neither partial nor complete recovery is highly probable. **Objective:** To analyze global scientific production and identify research hotspots related to PPCM. **Methods:** The keyword “peripartum cardiomyopathy” was used to retrieve articles from Scopus database. A total of 509 articles were extracted. We used Scopus database analysis report and VOSviewer (version 1.6.18) to analyze annual publication number, country, citation and H-index, authors, institution, source journal, reference, and research hotspot. **Results:** The trend of annual publication numbers has increased significantly, with the United States leading the amounts of publication and H-index in PPCM study. Hilfiker-Kleiner, D. contributed the most publications and the most active institution was Medizinische Hochschule Hannover MHH. By employing an overlay visualization, we shed light on the evolving research emphases, wherein prominent topics such as “diagnostic imaging” and “practical guidelines” have emerged as major areas of focus in recent years. **Conclusion:** From 1971 to 2022, numbers of publications in PPCM research have increased gradually, and this trend is predicted to keep arising. Recent studies are becoming more focused on diagnostic imaging and practical guidelines. In the future, expanding global collaboration and conducting more in-depth studies are needed.

Keywords: Peripartum cardiomyopathy, Bibliometric analysis, VOSviewer.

1. BACKGROUND

Peripartum cardiomyopathy (PPCM) is a myocardial disease associated with pregnancy. The onset comprising from the last month of pregnancy until five months postpartum (1). The diagnostic criteria are development of heart failure (HF) in the last month of pregnancy to five months postpartum, no other possible etiology of HF, and no history of heart disease prior to last month of pregnancy (2). Symptoms associated with PPCM are highly variable including fatigue, dyspnea, orthopnea, palpitations, edema, chest pain, decreased endurance in exercise, and abdominal discomfort due to liver congestion (1). Complications such as thromboembolism, arrhythmia, and chronic cardiomyopathy can occur if treatments are not maximized (3). Poorly understood pathophysiology and difficulties in diagnosis may cause

PPCM to be underestimated (4). PPCM has a high morbidity and mortality, however the probability of partial nor full recovery are high. Guidelines are essential in treating PPCM patients respecting contraindications during pregnancy and lactation (5). Future research and studies regarding drug therapy and long-term outcomes are also needed (6).

Bibliometric analysis is a well-known method for analyzing and exploring scientific data (7). Bibliometric analysis facilitates authors to explore the contributions and work that has been performed to a certain field of research (8). This type of study also benefits researchers, policy makers, and stakeholders in improving the quality of their research and decisions. VOSviewer is one of bibliometric visualization tools for analyzing keywords, citations, authors, institutions and countries (9). The data

will be illustrated in a comprehensive map to provide insight about the trend of studies done regarding a certain topic. In this study, PPCM as the main topic will be used as a keyword for literature. Keywords distribution, co-citations, countries, and authors shown through bibliometric analysis can be analyzed.

2. OBJECTIVE

This research aims to analyze global scientific production and identify research hotspots related to PPCM; thus, the insight can be used to pilot further research that ought to be performed.

3. MATERIAL AND METHODS

Data Source and Search Strategy

The data was retrieved online through the Scopus database. Scopus is one of the largest global coverage publications, including journals, books, and conferences, to provide reliable scientific data. To prevent the bias brought on by the daily database updates, all searches were conducted on January 9th, 2023 with keyword 'peripartum cardiomyopathy'. The initial search showed a total of 2,382 studies. We restricted the literature to those in which the language was English and had completed the publication stage. In this study, only document type articles, reviews, and conference papers, with journals as the source type, were included. 722 studies met all of the requirements' criteria. Afterward, we screened all the studies that met our requirements through the title and abstract to exclude irrelevant studies. A total of 509 studies were downloaded and analyzed. We collected data regarding authorship, journal, institution, country, and keywords from each article.

Data Analysis

The downloaded data were analyzed using the Scopus database literature analysis report. Then, VOSviewer (version 1.6.18) was employed to analyze publication output. VOSviewer is a visualization software that displays cluster analysis and has an incredible visualization of data from various sources. Outputs are presented as nodes and links to view existing associations between bibliometric data. The size of the nodes is proportional to the frequency of occurrence. Furthermore, the distance between each node represents the strength of the association between the terms displayed.

4. RESULTS

Distributions of Annual Publications

In a total of 722 papers, only 509 papers met our criteria. Figure 1 shows the total number of publications by year, with a trend that shows a consistent upward movement from nine articles in 1970 to 509 articles in 2022. The first and second publications were published in 1971. The polynomial curve fitting of publication growth in PPCM research revealed a substantial association between publication year and number of publications (coefficient of determination (R^2) = 0.983). The number of publications is expected to exceed 600 by 2025, according to curve fitting.

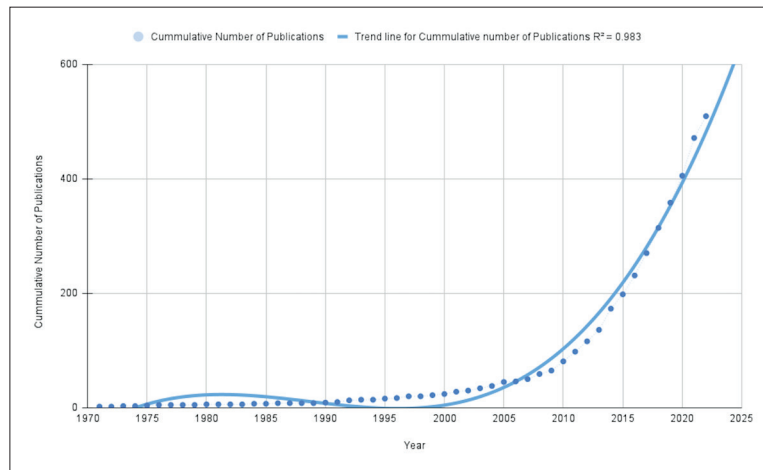


Figure 1. The trend of publications growth in PPCM study

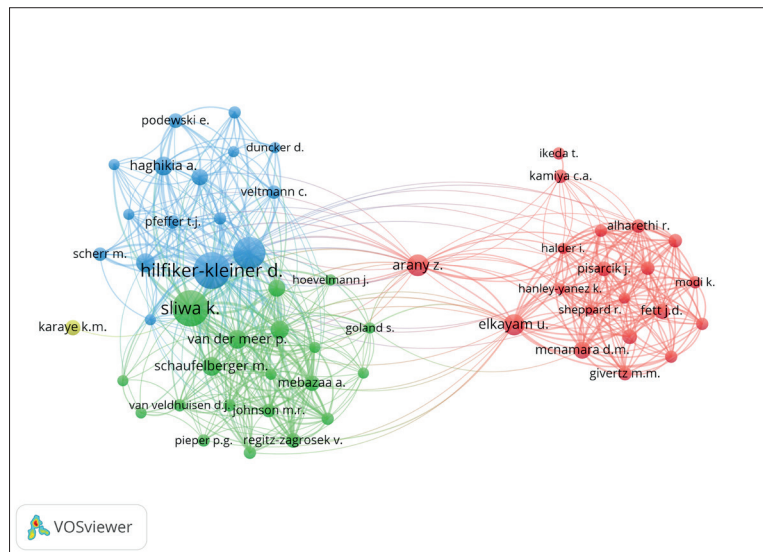


Figure 2. Author analysis of PPCM publications

Distribution of Country or Territories with Most Publications

The 509 publications included in the PPCM study were dispersed among 98 nations or territories. The United States published the most articles (169), followed by Germany (79), the United Kingdom (60), and South Africa (52). Japan, with 31 papers published, was the only Asian country to make the top 10.

Citations and H-index Analysis

According to a Scopus analysis, PPCM-related articles were cited 22,437 times between 1971 and 2022 (19,649 times without self-citations). Amongst the top 10 most productive countries and territories, the United States achieved the highest h-index (49) and sum of citations (9,981 times). Although Italy, Sweden, and France have less published articles compared to Japan, the H-index and sum of citations were found to be more impactful in this particular area.

Distributions of Authors with Most Publications

Amongst 509 journals, 44 publications were made by Hilfiker-Kleiner, D. Ranked second and third following Hilfiker, Silwa, K. made 43 publications and Bauersachs, J. made 34 publications. The later authors made a lower number of publications with Arany, Z. and Elkayam, U. with 16 publications each. Distribution analysis of authors shows a distribution of

Rank	Title	Journal	Year	Citations
1	2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death the Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC) Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC)	European Heart Journal	2015	2454
2	ESC Guidelines on the management of cardiovascular diseases during pregnancy	European Heart Journal	2011	1297
3	2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: A report of the American college of cardiology/American heart association task force on practice guidelines	Journal of the American College of Cardiology	2014	892
4	2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy	European Heart Journal	2018	869
5	Peripartum cardiomyopathy: National Heart, Lung, and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review	JAMA	2000	712
6	Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: A position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy	European Journal of Heart Failure	2010	652
7	Proposal for a revised definition of dilated cardiomyopathy, hypokinetic non-dilated cardiomyopathy, and its implications for clinical practice: A position statement of the ESC working group on myocardial and pericardial diseases	European Heart Journal	2016	533
8	Cardiovascular disease in women: Clinical perspectives	Circulation Research	2016	504
9	Natural course of peripartum cardiomyopathy	Circulation	1971	420
10	Pregnancy-associated cardiomyopathy: Clinical characteristics and a comparison between early and late presentation	Circulation	2005	413

Table 1. Top 10 references with the most citation frequency in PPCM study

author groups in PPCM studies. The distribution was made with five as the number of occurrences. The link between all nodes represents the relation between each author in publishing PPCM journal. The bigger the nodes the higher the number of journals published. From the cluster analysis from VOSViewer of authors, Arany, Z. shows a connection with all clusters (Figure 2). This elaborated list of authors can be a possible future connection for collaborators in producing new journals regarding PPCM.

Distributions of Institutions and Source Journals

Fifty-two publications related to PPCM are associated with Medizinische Hochschule Hannover (MHH). Ranked second is University of Cape Town with 41 publications related to PPCM. The subsequent rank of institutions shows a drop of over 20 journals with Universitair Medisch Centrum Groningen with 21 publications. The next ranks have similar numbers such as Faculty of Health and science and University of the Witwatersrand, Johannesburg with 19 and 18 publications consecutively.

According to the data that was retrieved, 180 journals received publications about PPCM study. Esc Heart Failure, a France journal, has been the most prolific, with 18 articles, followed by European Journal of Heart Failure (16 articles) and Circulation (14 articles), which both are United States journals.

Distribution of Cited References

Table 1 shows the top 10 cited articles on PPCM. The number of citations ranged from 413 for the article in tenth place to 2,454 for the leading article. Each of the 10 articles was cited over 400 times. Among these 509 articles, the two most frequently cited are from European Heart Journal.

Hotspots of PPCM Studies

The research hotspots of PPCM were determined by the co-occurrence analysis of high-frequency keywords. A keyword's minimum number of co-occurrences was set at 15.

Only 205 of the 4,289 PPCM-related keywords that were retrieved met the threshold. Several keywords that were irrelevant to the topic were removed. Following that, bibliometric analysis was performed to display the results based on frequently occurring keywords. The keywords with similarities were divided into four clusters, which were identified in Figure 3a as red, green, blue, and yellow, respectively. The nodes' sizes are linearly correlated with their frequency of occurrence. Therefore, the keyword with the lowest frequency, reflected by a smaller node, denotes that the study topic is still in its developmental stages and requires further research in subsequent studies (e.g., genetic predisposition, oxidative stress, carvedilol, bisoprolol, dobutamine, lung embolism, eclampsia, comorbidity, and C-reactive protein).

Figure 3b depicts an overlay visualization of the PPCM study according to the year of publication, from 1971 to 2022. In the early years of PPCM research, the main topics were myocardium (Average publication year [APY] = 2008.75), congestive heart failure (APY = 2009.9688), and cardiomyopathy (APY = 2010.3571). Lately the keywords became more focused on diagnostic imaging (APY = 2018.1944) and practical guidelines (APY = 2018.4706).

5. DISCUSSION

Between 1971 and 2022, the number of international publications on PPCM research increased significantly each year. We discovered that PPCM-related articles have consistently been published from the year 1999 through 2022, and the number of articles has a tendency to increase each year. We predicted that this trend would keep increasing since there are still a lot of areas to be developed. The highest institutions who published PPCM publications are mostly health related such as hospitals or faculty of medicine. PPCM is indeed a health issue that should be dove deeper, however other aspects such as economical and sociological can also be explored (10).

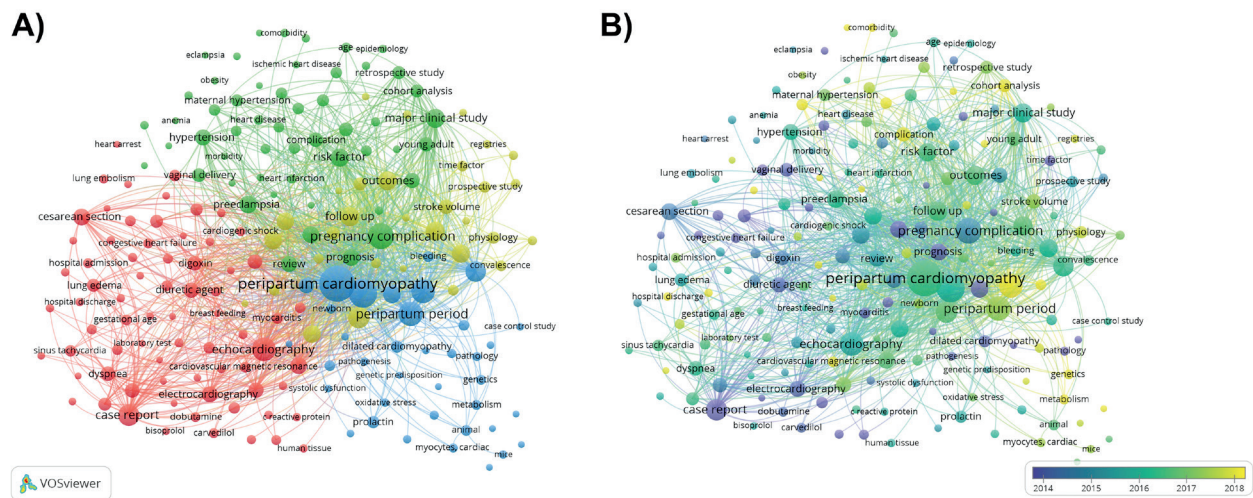


Figure 3. Hotspot of PPCM studies. a) co-occurrence network visualizations, b) co-occurrence overlay visualizations

The most productive country to publish articles-related to PPCM is the United States, followed by Germany, United Kingdom and South Africa. In terms of H-index and citation counts, the United States also held the top spots. This could be attributed to the fact that the United States is the world's highest GDP (11). As a result, the United States is able to support the required scientific research (12).

Although Japan was ranked as the top six most productive countries in terms of publications, Japan has less H-index and cited articles compared to several countries below them. This could be due to the fact that the most cited article titled '2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death the Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC) Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC)', fourth most cited article titled '2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy' and sixth most cited article titled 'Current state of knowledge on etiology, diagnosis, management, and therapy of peripartum cardiomyopathy: A position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy' were written by almost all European countries including writers from Italy, Sweden, and France. Therefore, this could contribute to the increase of H-index and sum of citations in these countries.

Publication scopes that are explored by the top 10 authors mostly were related to cardiomyopathy, peripartum period, and bromocriptine. Pathophysiology of the disease is highly discussed by the authors, but remains poorly understood (5). However, the latest evidence has substantially improved our knowledge of the condition. The two main hypothetical pathophysiology of PPCM are: a significant toxic role for late-gestational hormones on the maternal vasculature and genetic predisposition of PPCM (13). The absence of STAT3 in the heart plays a critical role in reducing the expression of manganese superoxide dismutase (MnSOD) which elevated secretion of reactive oxygen species (ROS). ROS triggers activation of cathepsin D, an extracellular peptidase that cleaves prolactin into 16-kDa, an angiostatic and pro-apoptotic sub

fragment (14). This leads to endothelial dysfunction and cardiomyocyte apoptosis. The PTHLH gene, that regulates vascular homeostasis and TTN gene, that encodes sarcomere protein titin are considered to be responsible for development of cardiomyopathy including dilated cardiomyopathy (DCM) and PPCM. However, this genetic correlation itself still remained unclear due to the different characterizations found in patients with DCM and PPCM (14).

Authors of prior PPCM publications discussed the possible treatment for PPCM as well. Bromocriptine is quite a dominant topic due to its potential ability as a disease-specific therapy for PPCM by blocking prolactin with the dopamine D2 receptor agonist (15,16). Bromocriptine, on top of standard HF therapy, may be beneficial to improve LV recovery and clinical outcome (17,18). There were no significant differences between the short-term (1 week of 2.5 mg bromocriptine once daily) and long-term (2.5 mg of bromocriptine twice daily for two weeks, then 2.5 mg once daily for six weeks) treatments (19). Bromocriptine must always be used in conjunction with heparin anticoagulation (LMWH or UFH) in at least a prophylactic dose (20,21).

Topics regarding other alternative remedies in treating PPCM such as left ventricular assist devices (LVAD) and additional usage of cabergoline with a similar effect to bromocriptine was also discussed (22,23). Current practical guidelines '2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy' suggest that in acute/subacute conditions, PPCM should be treated according to ESC acute HF guidelines, while avoiding fetotoxic agents (ACE inhibitors, ARNI, ARB, atenolol, and MRA) (17).

Prognosis of PPCM was discussed in several studies. Long term outcome of PPCM can result in full recovery, residual heart failure and even death. Subsequent pregnancies within one year after PPCM are at a substantial risk of relapsing and encourage death, hence PPCM patients should be monitored even one year postpartum (24). The impact of breastfeeding towards myocardial recovery post PPCM is also detrimental as a result of increased prolactin levels (25). A study analyzed the possibility of cancer in PPCM women and showed a 16-fold higher cancer development compared to same aged women. This is likely to be caused by cardiomyopathy or cancer predisposition syndrome which is triggered by PPCM (22).

6. CONCLUSION

We constructed a comprehensive review regarding the extent of PPCM study through the use of bibliometric analysis. Over the last decade, the number of publications in the PPCM study has increased significantly, and we predict this trend will keep rising. The United States has been the most productive and impactful country in terms of publication in PPCM study. Expanding global collaboration and conducting more in-depth studies in this area are needed. Through this study, we identify research hotspots in this field, along with research issues that are still in the stages of development, thus providing various insights for researchers in the future.

- **Acknowledgements:** The authors would like to express their gratitude to the anonymous reviewer and editor who contributed in improving the quality of this paper.
- **Authors contribution:** MAW, MFI, and RM were involved in the study conception and design. MAW, GAL, and LADG reviewed search results and completed data extraction. MAW, GAL, LADG, and MFI performed data analysis and interpretation. MAW, GAL, LADG, and RM drafted the manuscript, then MAW, MFI, and RM critically revised it. All authors provided their final approval for the to-be-published version and agreed to be held accountable for all aspects of the work.
- **Patient Consent Form:** Patient consent form was not required in this study.
- **Author's contribution:** All authors of this article were involved in all steps of preparation of this article. Final proofreading was made by the first author
- **Conflict of interest:** None declared.
- **Financial support and sponsorship:** This study was supported by grant-in-aid from Faculty of Medicine, Universitas Sebelas Maret, Universitas Sebelas Maret Hospital, and Lembaga Penelitian dan Pengabdian Masyarakat (LPPM) Universitas Sebelas Maret.

REFERENCES

1. Azibani F, Sliwa K. Peripartum Cardiomyopathy: an Update. Vol. 15, *Current Heart Failure Reports*. Current Science Inc.; 2018: 297–306.
2. Golland S, Elkayam U. Peripartum Cardiomyopathy. In: *Cardiac Problems in Pregnancy*, 4th Edition. Wiley; 2019: 128–54.
3. Honigberg MC, Givertz MM. Peripartum cardiomyopathy. Vol. 364, *BMJ* (Online). BMJ Publishing Group; 2019.
4. Hilfiker-Kleiner D, Haghikia A, Nonhoff J, Bauersachs J. Peripartum cardiomyopathy: Current management and future perspectives. Vol. 36, *European Heart Journal*. Oxford University Press; 2015: 1090–7.
5. Bauersachs J, König T, van der Meer P, Petrie MC, Hilfiker-Kleiner D, Mbakwem A, et al. Pathophysiology, diagnosis and management of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Study Group on peripartum cardiomyopathy. *Eur J Heart Fail*. 2019 Jul 1; 21(7): 827–843.
6. Davis MB, Arany Z, McNamara DM, Golland S, Elkayam U. Peripartum Cardiomyopathy: JACC State-of-the-Art Review. Vol. 75, *Journal of the American College of Cardiology*. NLM (Medline); 2020: 207–21.
7. Skaf L, Buonocore E, Dumontet S, Capone R, Franzese PP. Applying network analysis to explore the global scientific literature on food security. *Ecol Inform*. 2020 Mar 1; 56.
8. Donthu N, Kumar S, Mukherjee D, Pandey N, Lim WM. How to conduct a bibliometric analysis: An overview and guidelines. *J Bus Res*. 2021 Sep 1; 133: 285–296.
9. van Eck NJ, Waltman L. Citation-based clustering of publications using CitNetExplorer and VOSviewer. *Scientometrics*. 2017 May 1; 111(2): 1053–1070.
10. Amiya E. Social Inequalities in Non-ischemic Cardiomyopathies. Vol. 9, *Frontiers in Cardiovascular Medicine*. Frontiers Media S.A.; 2022.
11. Suzuki E, Koh WC, Baffes J. World Bank. 2023 [cited 2023 Jan 14]. World Bank Open Data. Available from: <https://data.worldbank.org>
12. Rodríguez-Navarro A, Brito R. The link between countries' economic and scientific wealth has a complex dependence on technological activity and research policy. *Scientometrics*. 2022 May 1; 127(5): 2871–2996.
13. Arany Z, Elkayam U. Peripartum cardiomyopathy. *Circulation*. 2016 Apr 5; 133(14): 1397–1409.
14. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: A position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Vol. 12, *European Journal of Heart Failure*. 2010: 767–778.
15. Sliwa K, Bauersachs J, Arany Z, Spracklen TF, Hilfiker-Kleiner D. Peripartum cardiomyopathy: From genetics to management. Vol. 42, *European Heart Journal*. Oxford University Press; 2021: 3094–3102.
16. Naz F, Malik A, Riaz M, Mahmood Q, Mehmood MH, Rasool G, et al. Bromocriptine therapy: Review of mechanism of action, safety and tolerability. *Clin Exp Pharmacol Physiol*. 2022 Aug 22; 49(8): 903–922.
17. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cifková R, de Bonis M, et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *European Heart Journal*. Oxford University Press; 2018; 39: 3165–3241.
18. Hoevelmann J, Engel ME, Müller E, Hohlfeld A, Böhm M, Sliwa K, et al. A global perspective on the management and outcomes of peripartum cardiomyopathy: a systematic review and meta-analysis. *Eur J Heart Fail*. 2022 Sep 26; 24(9): 1719–1736.
19. Hilfiker-Kleiner D, Haghikia A, Berliner D, Vogel-Claussen J, Schwab J, Franke A, et al. Bromocriptine for the treatment of peripartum cardiomyopathy: A multicentre randomized study. *Eur Heart J*. 2017 Sep 14; 38(35): 2671–2679.
20. Desplante O, Tremblay-Gravel M, Avram R, Marquis-Gravel G, Ducharme A, Jolicoeur EM. The Medical Treatment of New-Onset Peripartum Cardiomyopathy: A Systematic Review of Prospective Studies. Vol. 31, *Canadian Journal of Cardiology*. Pulsus Group Inc.; 2015: 1421–1426.
21. Haghikia A, Podewski E, Berliner D, Sonnenschein K, Fischer D, Angermann CE, et al. Rationale and design of a randomized, controlled multicentre clinical trial to evaluate the effect of bromocriptine on left ventricular function in women with peripartum cardiomyopathy. *Clinical Research in Cardiology*. 2015 May 31; 104(11): 911–917.
22. Pfeffer TJ, Schlothauer S, Pietzsch S, Schaufelberger M, Auber B, Ricke-Hoch M, et al. Increased Cancer Prevalence in Peripartum Cardiomyopathy. *JACC CardioOncol*. 2019 Dec 1; 1(2): 196–205.
23. Berliner D, Li T, Mariani S, Hamdan R, Hanke J, König T, et al. Clinical characteristics and long-term outcomes in patients with peripartum cardiomyopathy (PPCM) receiving left ventricular assist devices (LVAD). *Artif Organs*. 2022 Sep 27.
24. Sliwa K, Petrie MC, Hilfiker-Kleiner D, Mebazaa A, Jackson A, Johnson MR, et al. Long-term prognosis, subsequent pregnancy, contraception and overall management of peripartum cardiomyopathy: practical guidance paper from the Heart Failure Association of the European Society of Cardiology Study Group on Peripartum Cardiomyopathy. *Eur J Heart Fail*. 2018 Jun 1; 20(6): 951–962.
25. Koczo A, Marino A, Jeyabalan A, Elkayam U, Cooper LT, Fett J, et al. Breast-feeding, Cellular Immune Activation, and Myocardial Recovery in Peripartum Cardiomyopathy. *JACC Basic Transl Sci*. 2019 Jun 1; 4(3): 291–300.