COMMENTARY

OvaRePred: Redefing ovarian aging and pioneering the journey towards women's health management

Huiyu Xu,[1,3] Wei Wang,[1,3] Yong Han,[2] Rong Li,[1,*] and Jie Qiao[1,*]

[1]State Key Laboratory of Female Fertility Promotion, Center for Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing 100191, China

[2]Clinical Research Institute, Zhejiang Provincial People's Hospital, Hangzhou 310000, China

[3]These authors contributed equally

*Correspondence: roseli001@bjmu.edu.cn (R.L.); jie.qiao@263.net (J.Q.)

Received: February 9, 2024; Accepted: March 29, 2024; Published Online: April 10, 2024; https://doi.org/10.59717/j.xinn-med.2024.100068

Citation: Xu H., Wang W., Han Y., et al., (2024). OvaRePred: Redefing ovarian aging and pioneering the journey towards women's health management. The Innovation Medicine **2(2)**: 100068.

Ovarian reserve, a key determinant of female fertility, denotes the number of primordial follicles residing in the ovarian cortex that can mature into oocytes.[1] This reserve varies dramatically, spanning from thousands to millions at birth. Concurrently, the pace of ovarian aging remains relatively steady, resulting in notable differences in ovarian reserve among women of the same age.[1] As the ovarian reserve approaches depletion, women commonly transition into perimenopause, a phase where fertility is significantly diminished, often nearing complete depletion.

OvaRePred stands as a trailblazing AI tool in reproductive health, leveraging non-invasive parameters such as serum Anti-Müllerian hormone (AMH) and age to accurately gauge a woman's current ovarian reserve. Beyond assessment, it provides predictions for vital fertility milestones, including the age of Diminished Ovarian Reserve (DOR) and the initiation of perimenopause.[1] Here we aim to thoroughly examine its wide-ranging impact, scrutinizing every aspect of its practical utility.

FUTURE-ORIENTED OVAREPRED APPLICATIONS

Personalized fertility planning

OvaRePred provides a tailored evaluation of ovarian reserve, enabling individuals to gain insights into their fertility status by accurately measuring their current ovarian reserve. This becomes particularly vital for those intending to delay childbearing. By revealing their distinct ovarian reserve patterns, it allows them to strategically plan the optimal timing for conception, facilitating a well-balanced integration of their career aspirations and personal childbearing goals. The Peking University Third Hospital has begun the practice of providing OVARePred assessment results to all women undergoing AMH and FSH tests.

New standard for defining ovarian insufficiency

Premature Ovarian Insufficiency (POI) occurs when a woman's ovaries cease functioning normally before the age of 40, potentially leading to infertility and early menopause symptoms like hot flashes, vaginal dryness, and mood fluctuations. The goal of diagnosing POI is to enable proactive management of reproductive health, prevent and address related health issues, provide psychological support, and assist in family health planning.

The diagnosis of POI is challenged,[2] while the prospect of employing OvaRePred's ovarian reserve score as a substitute for conventional POI diagnostic criteria seems promising. This approach could benefit women both with and without POI, by advising the initiation of perimenopausal management anchored in ovarian function assessments. For instance, management could commence when the ovarian reserve score decreases to 25, which correspond to a state of near-complete fertility loss. Although OvaRePred's ovarian reserve score is promising as an alternative for current POI definition and has the potential to improve health management for more women, establishing precise thresholds for these scores requires more comprehensive research and substantiation.

Perimenopausal management

OvaRePred predicts the onset age of perimenopause, a crucial transition in a woman's life marking the shift from reproductive to non-reproductive years. This phase is characterized by symptoms such as irregular periods, hot flashes, mood changes, sleep issues, and changes in sexual desire, stemming from reduced ovarian function and fluctuating estrogen levels. Other possible experiences include urinary problems, osteoporosis, skin changes, heart disease, mental disorders, diabetes, and weight gain. The intensity and duration of these symptoms vary among women.

OvaRePred offers an invaluable service by precisely predicting the onset age of perimenopause. This allows women to prepare effectively, both in body and mind, and to adopt proactive health management strategies in advance. Moreover, OvaRePred plays a crucial role in enhancing awareness about health issues related to perimenopause. Utilizing this tool, women can gain a thorough understanding of perimenopause's impact and explore effective approaches to navigate this intricate phase of life.

OvaRePred and dementia management

OvaRePred,[1] together with the ADpred model,[3] our advanced dementia prediction tool, offer significant insights into women's health. The ADpred model is adept at forecasting Alzheimer's Disease (AD) dementia, Lewy body dementia, vascular dementia, as well as mild cognitive impairment. Considering the higher prevalence of dementia in elder women compared to elder men, the reduction in ovarian hormone levels caused by menopause seems to play a pivotal role in this phenomenon. Thus, hormone replacement therapy (HRT) during perimenopause may serve as an effective preventative approach against dementia, although its effectiveness is subject to ongoing debate. The potential ineffectiveness of HRT might largely be linked to the timing of HRT initiation.[4] After all, HRT is ineffective if the treatment started 10 years after menopause.

By determining the onset age of perimenopause by OvaRePred, this combination enables the tailored timing of HRT initiation, providing a more personalized approach to patient care. It is also instrumental in enhancing public awareness of dementia and menopause, promoting a societal shift towards healthier lifestyles and preventive measures. While promising, it's important to recognize the need for improved predictive accuracy and ongoing tool refinement to better serve dementia prevention and treatment efforts.

OvaRePred in Conjunction with Radiotherapy and Chemotherapy

Evaluating ovarian reserve both before and after chemoradiotherapy is essential, as these treatments can detrimentally impact a woman's fertility, resulting in ovarian insufficiency or premature menopause. OvaRePred serves as a valuable tool for gauging the potential effects of chemotherapy and radiotherapy on women's ovarian function. Utilizing OvaRePred's assessments, doctors can more effectively tailor radiotherapy and chemotherapy plans, prioritizing ovarian function preservation, particularly for patients wishing to conceive in the future. OvaRePred facilitates long-term tracking and management of ovarian health in these patients, providing continuous updates on ovarian reserve and aging pace, and guiding further treatment and recuperation, and aiding in maintaining optimal reproductive health post-treatment, including perimenopausal management and necessary psychological and social support. In conclusion, OvaRePred offers a novel approach for evaluating ovarian reserve and fertility function in patients undergoing chemotherapy and radiotherapy.

Others

The OvaRePre tool features a built-in algorithm equipped with an aging curve that is effective for the majority of women. However, for patients with ovarian diseases, their aging trajectories may diverge from the norm. To optimize OvaRePred's effectiveness in managing these patients, a future enhancement could involve tailoring its internal algorithm to accommodate

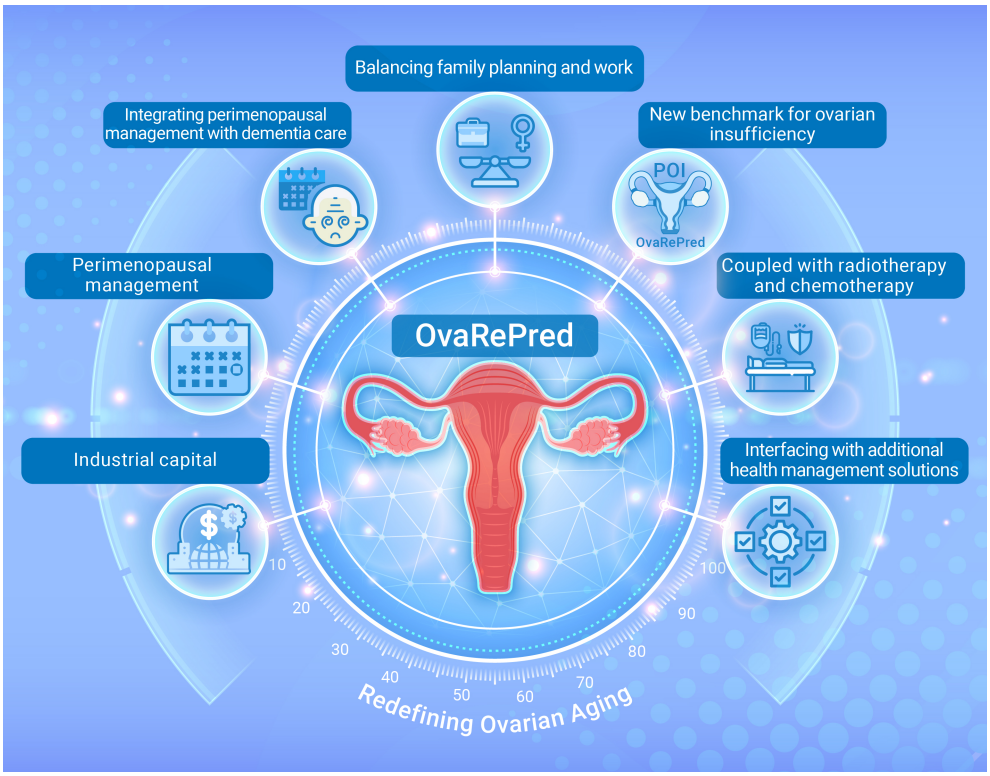

Figure 1. OvaRePred redefines ovarian aging
OvaRePred offers more than just an assessment of current ovarian reserve; it also predicts the timing of key fertility milestones in the future. Its applications are diverse and impactful, ranging from the development of personalized fertility plans to facilitating a balance between work and personal life, and improving health management for women during perimenopause. Significantly, OvaRePred is instrumental in demystifying the relationship between hormone replacement therapy in perimenopause and the risk of dementia, thereby aiding in the development of more effective dementia prevention methods. The OvaRePred-defined ovarian reserve score has the potential to supersede existing diagnostic criteria for Premature Ovarian Insufficiency (POI), offering benefits to a broad spectrum of women, not limited to those experiencing premature aging. OvaRePred is also indispensable for evaluating ovarian reserve both before and after undergoing radiotherapy and chemotherapy. Integrated with other health management instruments, OvaRePred is poised to substantially improve women's healthcare. Most crucially, OvaRePred has the potential to bridge the gap between medical knowledge and industrial investment, paving the way for innovative breakthroughs in healthcare.

the distinct data profiles of various disease groups. This customization would make OvaRePred more applicable to diverse groups, including individuals with conditions like Polycystic Ovary Syndrome, and those undergoing varied radiotherapy and chemotherapy treatments.

The management of ovarian disease necessitates a multidisciplinary approach, involving experts such as gynecologists, endocrinologists, and reproductive medicine specialists. OvaRePred can facilitate this collaborative effort by enabling these professionals to exchange and analyze data, thereby crafting more holistic and tailored treatment strategies. Additionally, OvaRePred functions as an informative resource to enhance reproductive health awareness. By offering concrete data on ovarian reserve, fertility, and the natural aging process of the ovaries, it fosters enriched dialogues between patients and healthcare providers, leading to more informed healthcare decisions.

In the realm of scientific research, OvaRePred is a treasure trove of invaluable data. It enables extensive longitudinal studies in areas such as fertility, aging, and the impact of different interventions. The insights gained from these data have the potential to drive forward progress in reproductive medicine, paving the way for treatments that are both more effective and personalized. Looking ahead, integrating OvaRePred's data with other pertinent health metrics—like hormone levels, menstrual cycle regularity, environmental factors such as air pollution, and lifestyle aspects including diet and exercise—could offer a more holistic approach to health management.

On a wider scale, OvaRePred, potentially integrated with other tools in the future, holds the promise of significantly influencing the social and economic facets of fertility. By enabling individuals to more effectively plan their families, it can impact areas such as workforce planning, parental leave policies, and the allocation of health resources. Furthermore, early intervention in reproductive health has the potential to decrease healthcare costs and enhance the overall efficiency of the healthcare system.

Regarding the limitations of OvaRePred, it's crucial to understand that its predictions are shaped by broad population standards and might not extend accurately to everyone. Hence, our findings should predominantly serve as guidance for women of reproductive age rather than a definitive diagnostic criterion.

INTEGRATION OF OVAREPRED AND INDUSTRIAL CAPITAL

Collaborating with industrial capital is of paramount importance.[5] Industrial capital can offer the vital financial backing necessary for the research, development, and dissemination of OvaRePred. This encompasses financing additional clinical trials, technological advancements, marketing initiatives, and user education. OvaRePred can be assimilated into health management platforms or applications to deliver comprehensive services. By collaborating with electronic health record systems, online medical consultation services, or personal health record applications, we leverage industry capital resources and networks to broaden market reach, heighten public awareness of women's health, and instruct users on the effective utilization of these tools.

CONCLUSION

OvaRePred is at the cutting edge of a paradigm shift in reproductive medicine, moving towards a more personalized, predictive approach in healthcare. Its proficiency in assessing and predicting ovarian reserve status lays the groundwork for tailored patient care, well-informed choices, and an enhanced quality of life. Presently, OvaRePred is being adopted as a standard practice in numerous hospitals and health examination centers in China, including our own, and is expected to see a rapid expansion throughout China. As its utilization grows, OvaRePred is set to profoundly enrich our comprehension of fertility and perimenopause, ultimately leading to superior health management for people around the world. This breakthrough represents far more than a monumental advance in medical technology; it ushers in an era of enhanced empowerment and self-determination in the realm of reproductive health (Figure 1).

REFERENCES

1. Xu, H.Y., Feng, G.S., Yang, R., et al. (2023). OvaRePred: Online tool for predicting the age of fertility milestones. The Innovation **4**: 100490. DOI: 10.1016/j.xinn.2023.100490.
2. Armeni, E. (2022). Diagnostic challenges in suspected premature ovarian insufficiency. Case Rep Womens Hlth **5**: e00453. DOI: 10.1016/j.crwh.2022.e00453.
3. Xu, H., Feng, G., Li, R., et al. (2023). ADpred: A non-invasive model for three types of dementia and mild cognitive impairment. The Innovation Medicine **1**: 100026. DOI: 10.59717/j.xinn-med.2023.100026.
4. Whitmer, R.A., Quesenberry, C.P., Zhou, J.F., et al. (2011). Timing of hormone therapy and dementia: The critical window theory revisited. Ann Neurol **69**: 163–169. DOI: 10.1002/ana.22239.
5. Xu, H. (2023). The Innovation Conference 2023 for Medicine: Fostering collaborative solutions through thought-provoking questions. The Innovation Medicine **1**: 100044. DOI: 10.59717/j.xinn-med.2023.100044.

DECLARATION OF INTERESTS

Jie Qiao and Rong Li, as The Innovation Medicine Editorial Board members, were not involved in the manuscript's review or decision. Peer review was conducted independently. The other authors declare no competing interests.