Developing the ‘OCRAT’ Progressive Web Application (PWAs) for assessing ovarian cancer risk strategies

Nguyen Hoang Bach[1,3*], Tran Doan Tu[2], Nguyen Vu Quoc Huy[2]
(1) Department of Microbiology, Hue University of Medicine and Pharmacy, Hue University
(2) Department of Obstetrics and Gynecology, Hue University of Medicine and Pharmacy, Hue University
(3) Center for Information Technology, Hue University of Medicine and Pharmacy, Hue University

Abstract

Introduction: Early prediction of ovarian cancer has not been given much attention, the application of combined models in clinical practice is not widespread, and the calculation of these models is still difficult due to the complexity and multiple variables. we have developed a PWA (Progressive Web Apps) application called OCRAT (Ovarian Cancer Risk Assessment Tools - Ovarian Cancer Risk Assessment Tools) with the goal of simplifying the calculation, contributing to increasing the ability to apply these models in clinical practice, teaching, and scientific research. **Materials and methods:** We used Progressive Web App (PWA) to build the app including four distinct models ROMA, CPH-I, RMI 4, and ADNEX. **Results:** The app called OCRAT composes 3 main functions: ROMA&CPH-I, RMI 4, and ADNEX can install and run properly in any operating system. The app was officially announced at the Vietnam National Conference of Obstetrics & Gynecology 2023. **Conclusions:** This application has been widely introduced to specialized obstetricians and gynecologists and has received positive feedback due to the application’s convenience, accuracy, and ease of access.

Keywords: *ovarian cancer, ROMA, CPH-I, RMI 4, ADNEX, OCRAT.*

1. INTRODUCTION

Cancer is one of the major non-communicable diseases, a major challenge of the 21st century, undermining global economic development and threatening the achievement of the Millennium Development Goals. In women, ovarian cancer is one of the ten most common types of cancer, a dangerous type of cancer, that is considered a “silent killer” because it has the highest mortality rate and the worst prognosis of all reproductive cancers. The mortality rate has not changed in the past 30 years, and it is predicted that in 2040 this rate will increase significantly. Because 70% of ovarian cancers are diagnosed at an advanced stage (stage III/IV), when the disease has spread and invaded the pelvis and abdomen, the 5-year survival rate is 20 - 25%, while if detected at an early stage, this rate can be up to 90%. This makes treatment difficult and expensive, affecting the patient’s quality of life and prognosis. Therefore, early detection of ovarian cancer is of great importance.

In the past few decades, scientists around the world in the fields of molecular biology, cancer, obstetrics and gynecology, epidemiology, etc., have made great efforts to develop biomarkers, combined with imaging techniques (ultrasound, computed tomography (CT) scans, etc.), to create many combined models to increase predictive value. Some optimal models have been introduced and proven to be valuable, including the ROMA® algorithm, Copenhagen index (CPH-I), RMI index, and ADNEX® model. The ROMA® algorithm was developed by Fujirebio Diagnostics Inc., Tokyo, Japan in 2010 and was recommended for clinical practice by the U.S. Food and Drug Administration (FDA). In 2015, Karlsen et al. developed the Copenhagen index. While these two models are based on biomarkers (CA125, HE4) and patient characteristics (menopausal status and age), the RMI index and the ADNEX model are a combination of biomarkers (CA125) and ultrasound features of the tumor. Based on the results of research and international publications on the value of these indicators, international obstetrics and gynecology associations have issued recommendations on how to approach stratification and early detection of ovarian cancer.

In Vietnam, most ovarian cancers are diagnosed at an advanced stage, with a high mortality rate. Early prediction of ovarian cancer has not been given much attention, the application of combined models in clinical practice is not widespread, and the calculation of these models is still difficult due to the complexity and multiple variables.

Progressive web applications (PWAs) are a

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promising technology for healthcare because they offer a number of advantages over traditional native apps. PWAs are more secure, reliable, and accessible, and they can be installed on any device with a web browser. This makes them ideal for use in patient portals, remote patient monitoring, education and training, and clinical decision support. PWAs can be used to create patient portals that allow patients to access their medical records, schedule appointments, and communicate with their doctors. This can improve patient engagement and satisfaction, and it can also help to reduce costs. PWAs can also be used to collect data from patients remotely, such as their vital signs or blood sugar levels. This data can then be used to monitor patients' health and provide early intervention if necessary. This can improve patient outcomes and reduce the risk of complications. PWAs can also be used to create educational and training materials for healthcare professionals. This material can be accessed on any device, regardless of the operating system. This can make it easier for healthcare professionals to stay up-to-date on the latest medical knowledge [1,2].

Based on these problems, we have developed a PWA (Progressive Web Apps) application called OCRAT (Ovarian Cancer Risk Assessment Tools - Ovarian Cancer Risk Assessment Tools) with the goal of simplifying the calculation, contributing to increasing the ability to apply these models in clinical practice, teaching, and scientific research.

2. MATERIALS AND METHODS

2.1. Materials

ROMA® and CPH-I

Moore et al. 2009 developed an ovarian malignancy risk algorithm (ROMA) by integrating CA125, serum HE4 values, and menopausal status [3]. ROMA assesses patients into two groups: high-risk and low-risk. In 2011, the FDA recommended the use of the ROMA algorithm in clinical practice to help stratify ovarian cancer risk. The ROMA algorithm was calculated as follows:

ROMA Value (%) = exp(PI) / [1 + exp(PI)] × 100

In which, PI (Predictive Index) is the predictive index calculated as follows:

- Premenopausal *PI = –12 + 2.38 × LN[HE4] + 0.0626 × LN[CA125]*

- Postmenopausal *PI = –8.09 + 1.04 × LN[HE4] + 0.732 × LN[CA125]*

Karlsen et al. 2015 developed the Copenhagen Index by integrating biomarkers CA125, serum HE4, and patient age to assess the malignancy risk of ovarian tumors before surgery [4]. The CPH-I was calculated as follows:

$$\text{CPH-I} = -14.0647 + 1.0649 \times \log2(\text{HE4}) + 0.6050 \times \log2(\text{CA 125}) + 0.2672 \times \text{Age}/10$$

Predicted probability $PP = e^{(CPH-I)}/(1+e^{(CPH-I)})$

RMI 4

Jacobs et al., 1990 originally developed the RMI, which we have termed: RMI 1. Tingulstad et al. 1996 developed their version of the RMI and it is known as RMI 2. Tingulstad et al., 1996 modified the RMI, which we have termed: RMI 3. Yamamoto et al., 2009 created a new model of a malignancy risk index by adding the parameter of the tumor size score (S) to the RMI and termed it the RMI4 [5]. The RMI 4 was calculated as follows:

RMI 4 = U × M × S × CA125

Which, U is the ultrasound score, M is the menopausal score, and S is the tumor size score.

ADNEX®

Van Calster et al., 2014 developed a prediction model that is able to discriminate between five types of adnexal tumor (benign, borderline, stage I cancer, stage II-IV cancer, and secondary metastatic cancer), while still showing excellent overall discriminative capacity between benign and all malignant tumors [6]. The ADNEX® model includes nine variables: age (years), serum CA 125 level (U/mL), type of center (oncology center/other hospital), maximum diameter of the lesion (mm), proportion of solid tissue (%), number of papillary projections (0/1/2/3/> 3), more than 10 cyst locules (yes/no), acoustic shadow (yes/no) and ascites (yes/no). The outcome of this model is an absolute risk estimate (expressed as a percentage) for five different types of adnexal pathology: benign, borderline, Stage-I invasive, Stage-II–IV invasive, and secondary metastatic. Furthermore, a risk estimate for the overall risk of malignancy is given (which is the sum of the estimates for all subtypes of malignancy). A cut-off of ≥ 10% for the overall risk of malignancy was used to predict malignancy.

2.2. Methods

We use Progressive Web Apps (PWAs) technology to help web apps operate on different platforms as a "native mobile app". PWAs represent a transformative paradigm in modern web development. These web applications harness the power of advanced web technologies to offer users a native app-like experience directly within their web browsers [7]. PWAs leverage service workers to enable offline functionality, ensuring reliability and resilience, even in low or unstable network conditions. Their responsiveness across diverse devices and platforms, coupled with the ability to be installed on a user's home screen, blurs the line between web and native apps. This innovative approach not only simplifies app distribution but also enhances user engagement. Furthermore, PWAs are characterized by their improved security through HTTPS, fostering trust in online interactions. As PWAs continue to evolve and gain traction, they hold immense promise for the future of web applications, reshaping the way we interact with digital content and services [8].

In the development of the OCRAT application, JavaScript is employed to facilitate the computation of complex algorithms such as ROMA, CPH-I, RMI 4, and ADNEX. These algorithms are utilized for the purpose of integrating sophisticated calculations into the OCRAT platform. Depending on the specific parameters entered by users, JavaScript dynamically transmits these input values to the respective algorithms, initiates the computational processes, and subsequently provides users with the computed results. This approach enables the application to offer tailored and precise outcomes based on user-defined input (Figure 1).

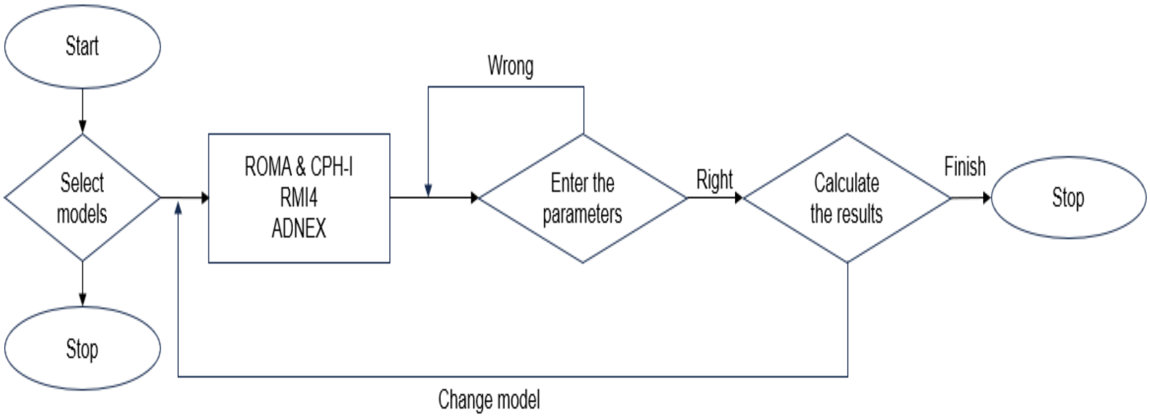

Fig 1. The diagram depicts the workflow of JavaScript to facilitate the computation of OCRAT's complex algorithms

3. RESULTS

Install the "OCRAT" PWAs

We have built the necessary and optimal components for the PWAs application in OCRAT so that it can be installed and function optimally for all platforms such as mobile devices such as phones, and tablets. It is currently hosted on the server of Hue University of Medicine and Pharmacy, accessible at the URL: https://ocrat.huemed-univ.edu.vn. OCRAT can be installed on different operating systems such as iOS, Android, Windows, and MacOS (Figure 2) with the following components:

- Web App manifest: The JSON manifest file (web app manifest) is a description of the application, defining information such as name, application logo, description, colors, and other settings.

- Service worker: JavaScript code that runs in the background in the browser, allowing the application to work offline and managing the caching of resources (like CSS files, images, JS) to help speed up page loading and minimize dependency on the network connection.

- Responsive web design: Make sure the application has a responsive design, meaning it can adapt and display well on different devices such as mobile phones, tablets, and desktop computers.

- HTTPS: PWAs require the use of the HTTPS protocol to ensure the safety and security of data transmission between client and server. This is also required by the browser to install Service Worker.

- App shell architecture: Uses App Shell architecture to load basic parts of the app (like address bar, navigation menu, app logo) quickly from the cache and then load specific content data possible from the server.

- Automatic updates: There is an automatic update mechanism to ensure users always use the latest version of the application through version declaration in Service Worker.

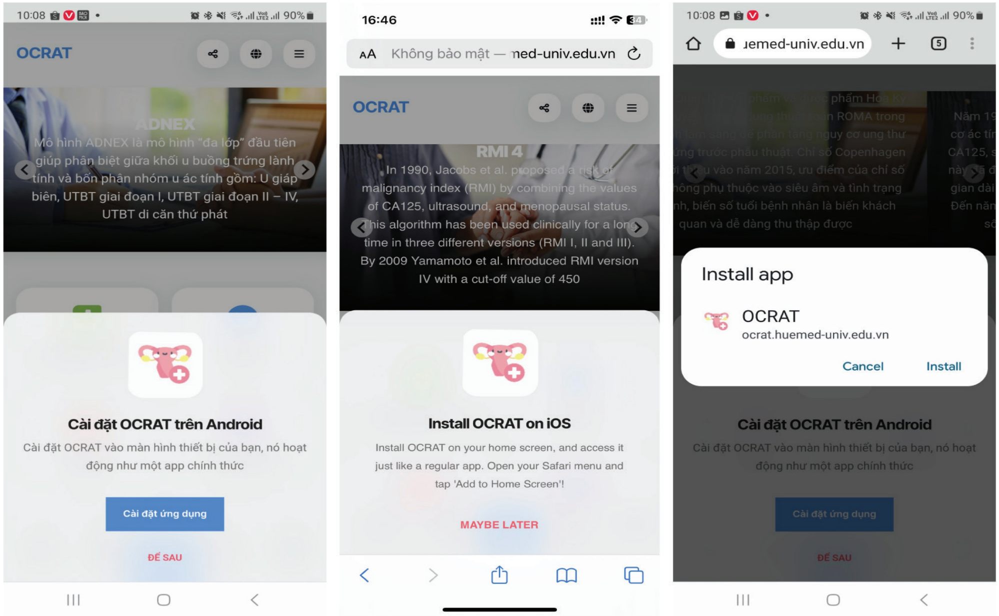

Fig 2. Install OCRAT PWA apps on iOS and Android device

User interface

Share tool and multiple language function

OCRAT is integrated with an application sharing library across information channels as a "native app" by calling the library of messaging applications such as Zalo, Viber, WhatsApp, contacts, email... Screen capture function, send a link directly from the device. OCRAT allows displaying application content in two different languages, whereby users can choose the language appropriate to the country and region to use (Figure 3).

Term annotation and references

The terms used in the application are supported with the annotation function by clicking on the terms and parameter names used in OCRAT. In the context of the increasingly developing world of information technology and science, ensuring the accuracy and legitimacy of algorithms and applications is extremely important. References in each research work not only help identify the source of information but also play an important role in ensuring reliability and scientific evidence for the application (Figure 3).

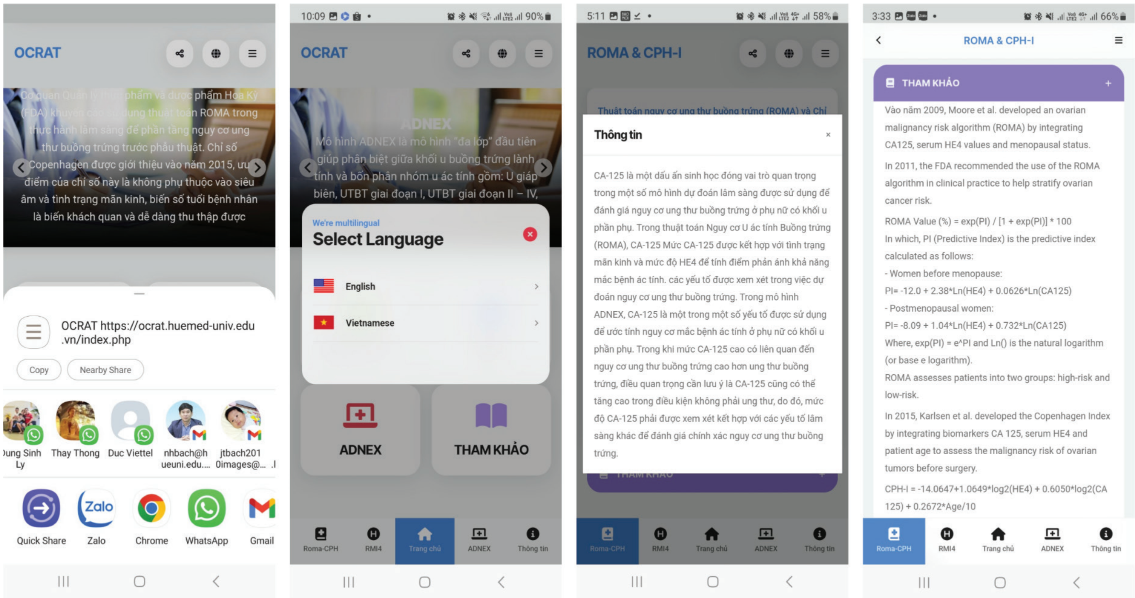

Fig 3. Share tool, multiple language, annotation and reference function

Validate input data

To optimize the way to enter data into applications such as age, concentration of biomarker, etc., we have optimized the data entered into the form to be characters or numbers or to warn about unreasonable parameters such as age between 20-80 years old.

Main functions

Ovarian cancer risk algorithm (ROMA) and Copenhagen index (CPH-I)

Existing applications all use two separate models, either ROMA or CPH-I. This is quite difficult for users when they want to consider predicted risks based on common biological indicators. OCRAT has combined the above two models into a single function: ROMA&CPH-I to provide complete information for both prediction models based on 4 main parameters: patient's age at examination, CA-125 concentration (U/mL), HE4 concentration (U/mL), menopausal status.

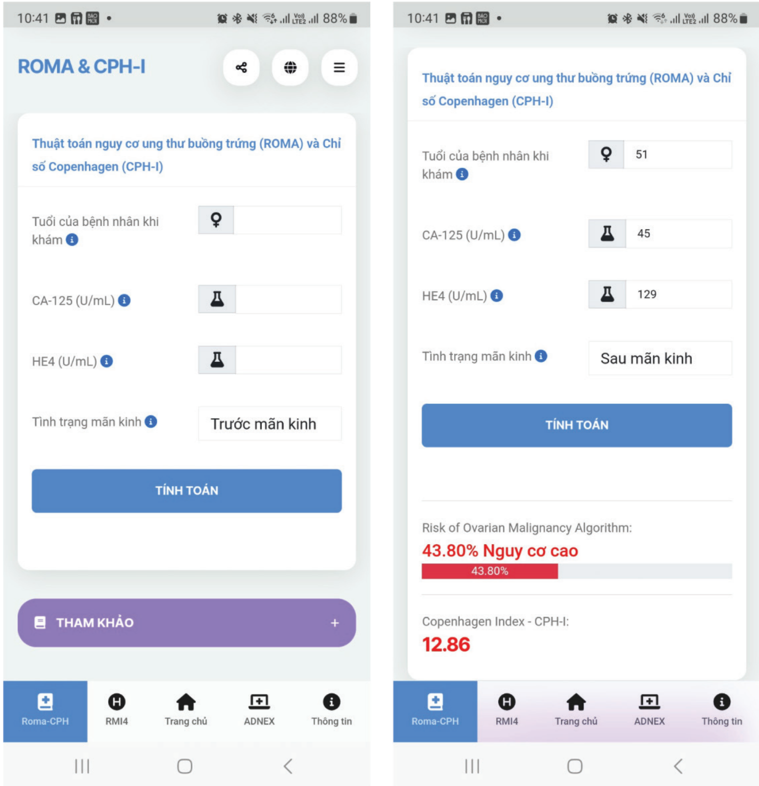

Fig 4. Interface and main functions of ROMA & CPH-I

The function allows changing input parameters and displaying real-time results without the need for a "calculate" command to display the results of 2 risk indicators. For the ROMA model, the function displayed in green and red corresponds to low or high risk on a bar graph according to percentage. Below is the calculated risk according to the CPH-I model (Figure 4).

RMI 4 ovarian cancer risk index calculator

Risk of Malignancy Index (RMI) is a scoring system for assessing the risk of ovarian cancer. It is a tool to help medical professionals, especially obstetricians, gynecologists, and oncologists, make smarter decisions about further management and surgical interventions that may be necessary. The RMI looks at three key factors that have been identified as important indicators for ovarian cancer: menopausal status, serum CA125 concentration, and ultrasound results. Function to build a tool to input the above parameters and an algorithm to calculate the RMI index and cut-off threshold of 450 according to version 4 (RMI4). With a risk greater than 450, the application will warn "High risk" in red and vice versa "Low risk" in green (Figure 5).

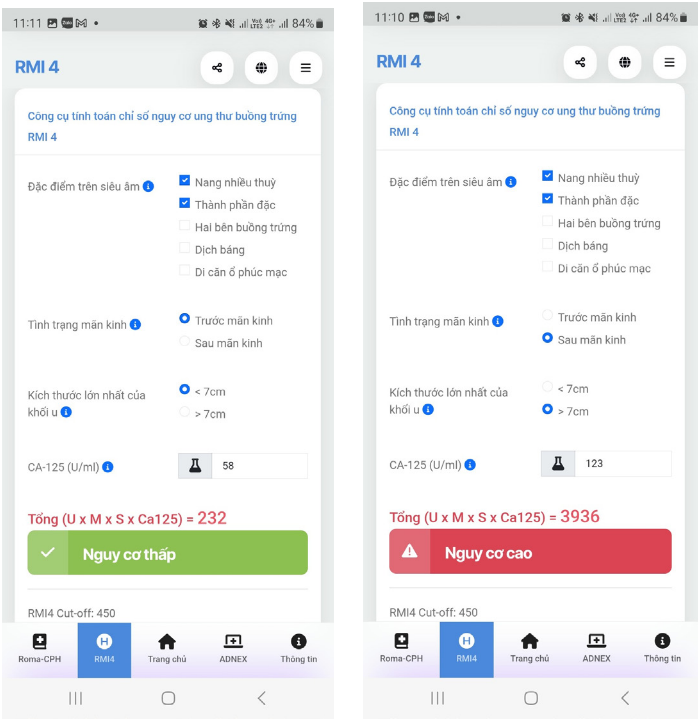

Fig 5. Interface and main functions of RMI 4

ADNEX model

ADNEX is a progressive prediction model and determination of ovarian tumor malignancy, developed by the University of Leuven (KU Leuven) in Belgium. Introduced in 2016, ADNEX is one of the most popular and effective ovarian tumor classification tools in the field of imaging medicine and gynecological oncology. The goal of ADNEX is to evaluate the probability of an ovarian tumor being benign or malignant based on imaging information from ultrasound and the clinical description of the tumor.

When using ADNEX, obstetricians, gynecologists, and medical specialists will provide information about the tumor from the patient's ultrasound and clinical presentation. Based on this information, the ADNEX model calculates and provides the expected probability of tumor malignancy (Figure 6).

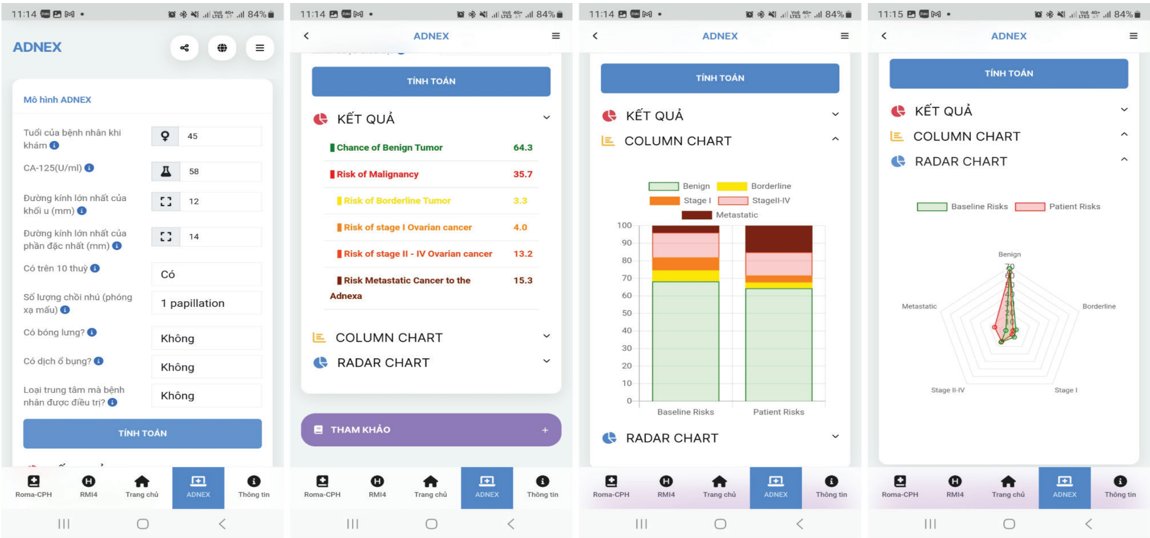

Fig 6. Interface and calculation results according to the ADNEX model: the risk data table, bar chart, and radar chart

Some of the benefits of ADNEX are that it helps doctors make more accurate treatment decisions, reduces the need for unnecessary surgeries, and reduces diagnostic redundancy. However, as with any diagnostic tool, ADNEX has limitations and should be used in conjunction with the clinical knowledge and skills of medical professionals to make optimal treatment decisions for each patient.

Commitment to privacy and security

This Progressive Web App (PWA) is designed with user privacy and security in mind. We understand the importance of protecting the data and taking steps to ensure user information remains secure.

HTTPS Everywhere: We use HTTPS (Hypertext Transfer Protocol Secure) and SSL (Secure Sockets Layer) to encrypt all communication between user devices and our servers. This industry-standard protocol safeguards your data from interception by unauthorized parties.

No data collection: This PWA is designed to function without collecting any personal information from the user.

Secure coding practices: We adhere to strict secure coding practices to minimize vulnerabilities and potential security risks.

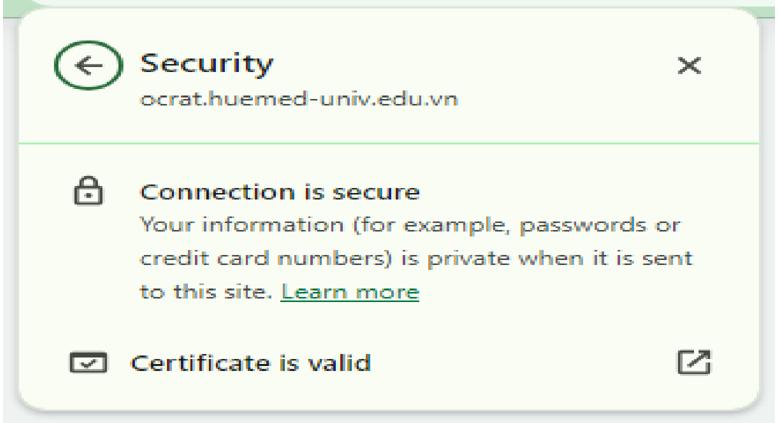

Fig 7. HTTPS and SSL on the OCRAT server

4. DISCUSSIONS

Web-based applications in healthcare have revolutionized the way medical professionals deliver care and patients access information. These applications, often referred to as health web apps, provide a versatile platform for a wide range of healthcare-related tasks [9].

OCRAT, our cutting-edge web-based application, is poised to make a significant impact in the realm of ovarian cancer risk assessment. With its user-friendly interface and robust functionality, OCRAT empowers healthcare professionals and individuals alike to swiftly and accurately assess ovarian cancer risk. Its four specialized models have been meticulously designed to provide precise risk calculations, enabling early detection and proactive management of this critical health concern. OCRAT's accessibility and convenience redefine the way we approach ovarian cancer risk assessment, offering a vital tool in the fight against this disease.

Ensuring the accuracy of risk predictions across OCRAT applications is of paramount importance to us. To address this concern, we have implemented rigorous measures. The formulas and algorithms utilized in our models are sourced directly from official reference materials. These references consist of research conducted by the original authors of these models, which have received recognition and validation from the wider community of scientists and clinicians specializing in the field of Obstetrics and Gynecology. Following the development of the calculation code based on these formulas and algorithms, we meticulously validate our calculations. To do so, we compare our results with established websites that utilize the same recognized indices to ensure accuracy. For the ADNEX model, we cross-verify our outcomes with those generated by the website located at: https://www.iotagroup.org/sites/default/files/adnexmodel/IOTA%20-%20ADNEX%20model.html. In instances where specific indicators lack an associated application or website for reference, we perform internal, independent assessments at each stage and within each group. This includes comparing our results with calculations conducted using widely accepted mathematical software like Excel and MATLAB.

These checks guarantee consistency and precision between our applications. By adhering to these stringent validation procedures, we aim to deliver the highest level of accuracy and reliability in our OCRAT applications, instilling confidence in both healthcare professionals and users.

OCRAT was officially announced at the 2023 Vietnam National Conference of Obstetrics and Gynecology 2023 by the Vice President of the Vietnam Association of Gynecology and Obstetrics. OCRAT was widely introduced to the member community of the Vietnam Obstetrics and Gynecology Association [10]. This shows the recognition of doctors specializing in Obstetrics and Gynecology about the scientific, convenience, and usefulness of OCRAT for clinical practice.

5. CONCLUSIONS

We have successfully developed the web-based app called OCRAT (Ovarian Cancer Risk Assessment Tools) based on the PWA technology including 4 models to calculate ovarian cancer risk. This application has been widely introduced to specialized obstetricians and gynecologists and has received positive feedback due to the application's convenience, accuracy, and ease of access.

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