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[1]V. M. Sineglazov,
[2]O. I. Chumachenko,
[3]S. O. Kolomoiets

DETERMINATION OF CHARACTERISTICS OF INFECTIOUS ENDOCARDITIS BASED ON INTELLIGENT PROCESSING OF ULTRASONIC IMAGES

[1]Aviation Computer-Integrated Complexes Department, Faculty of Air Navigation Electronics and Telecommunications, National Aviation University, Kyiv, Ukraine
[2,3]Faculty of Informatics and Computer Science, National Technical University of Ukraine "Ihor Sikorsky Kyiv Polytechnic Institute," Kyiv, Ukraine
E-mails: [1]svm@nau.edu.ua ORCID 0000-0002-3297-9060, [2]eliranvik@gmail.com ORCID 0000-0003-3006-7460, [3]serhii.o.kolomoiets@ukr.net ORCID 0000-0003-3741-4517

Abstract**—***The paper presents the pathogenetic factors in the development of infective endocarditis and identifies its predictors. The need for an echographic study associated with the search for the anatomical characteristics of infective endocarditis is shown: vegetation, destructive lesions (valve aneurysms, perforation or prolapse, etc.), the presence of abscesses, in the case of a prosthesis, a new divergence of the valve prosthesis may be a characteristic feature. A classification of research methods is presented that includes classical approaches of echocardiography (transthoracic, transesophageal) and new multidetector computed tomographic angiography and positron emission tomography with ^{18}F-fluorodeoxyglucose and the need for their use in different cases is determined. A block diagram of an intelligent diagnostic system for infective endocarditis has been developed. To process the obtained images in order to diagnose and determine the geometric dimensions, shapes, quantity, location, characteristics of infective endocarditis, it is proposed to use convolutional neural networks that allow solving the problem of image segmentation.*

Index Terms—Echocardiography; endocarditis; valve disease; intelligent processing; echographic images.

I. INTRODUCTION

Infective endocarditis (IE) is an inflammatory disease of the endocardium of infectious etiology, caused by the invasion of the pathogen into the valvular structures, endocardium, endothelium in the area of the main vessels adjacent to the heart, which is usually accompanied by bacteremia and damage to various organs and systems.

Infective endocarditis is associated with significant morbidity and mortality rates. In recent years, an increase in the incidence of IE has been recorded in various countries of the world. On average, IE occurs in 3.1–11.6 cases per 100,000 population. The prevalence of IE in different countries is not the same: in the USA – 3.8–15; in Canada, 2.0–2.5; in Sweden – 5.9; in England – 2.3–2.5; in France – 1.8–2.3; in Germany and Italy – 1.6 cases per 100,000 population. The epidemiological profile of the disease has changed significantly: the proportion of IE caused by staphylococci has increased, with a significant decrease in the role of streptococci in the development of the disease; the number of primary forms of IE increased, as well as the number of IE of prosthetic heart valves; there is an increase in the incidence of IE among the elderly and senile age. IE of prosthetic heart valves accounts for 7–25% of all cases.

Echocardiography plays a key role in the evaluation of infective endocarditis. It is useful for diagnosing endocarditis, assessing disease severity, predicting short- and long-term prognosis, predicting embolic events, and monitoring patients receiving specific antibiotic therapy. Echocardiography is also useful in diagnosing and managing the complications of IE, helping the physician make decisions, especially when considering surgical treatment. Finally, intraoperative echocardiography should be performed in IE to assist the surgeon in assessing and managing patients with IE during surgery. The current "Guidelines for the Practice of Echocardiography in Infective Endocarditis" are intended to provide an updated summary of the value and limitations of echocardiography in IE, as well as clear and simple guidelines for the optimal use of both transthoracic and transesophageal echocardiography in IE.

II. DANGER OF INFECTIOUS ENDOCARDITIS

Infective endocarditis is an potentially fatal damage to the heart valves and sometimes the linings of the chambers of the heart. This happens when germs (usually bacteria) from other parts of your body enter your bloodstream and attach to your heart valves and / or heart chambers. Infective endocarditis is also called bacterial endocarditis (BE) or acute, subacute (SBE), or chronic bacterial endocarditis.

The main pathogenetic factors in the development of IE include:

- damage to the endocardium;
- bacteremia;
- adhesion and reproduction of pathogenic bacteria on valves;
- weakening of the anti-infective protection of the macroorganism;
- development of heart failure;
- the formation of a systemic inflammatory response of the body.

Risk factors for poor outcomes are: the patient's condition (old age, prosthetic IE, insulin-dependent diabetes, the presence of concomitant pathology), the presence of complications of IE (heart failure, renal failure, septic shock, acute cerebrovascular accident, periannular complications), microorganisms (golden staphylococcus aureus, fungi, gram "–" m/o), echocardiographic signs (periannular complications, severe insufficiency of the aortic and/or mitral valve(s), left ventricular failure, pulmonary hypertension, large vegetations, severe prosthesis dysfunction, signs of increased diastolic pressure in the left ventricle).

Infective endocarditis may be suspected in the following situations:

1) the appearance of a new heart murmur;

2) thromboembolic syndrome with an unknown source;

3) sepsis with an unidentified source (especially when a pathogen typical for IE is detected);

4) fever, especially in patients with risk factors (Fever may be absent in elderly patients, after previous antibiotic therapy (ABT), in immunosuppressed patients, and in IE caused by low-virulence or atypical microorganisms):

- presence of intracardiac materials and devices (valvular prostheses, pacemaker, cardioverter defebrillator (CD), conduit);
- infective endocarditis in history;
- congenital or acquired heart defects;
- other conditions predisposing to IE (immunodeficiency states);
- predisposing recent interventions associated with bacteremia;
- episodes of congestive heart failure;
- conduction disturbances;
- a positive result of microbiological analysis of blood with the identification of a pathogen typical of IE or positive serological tests for chronic Q fever (microbiological findings may precede cardiac manifestations);
- vascular or immunological phenomena: embolism, Roth's spots, hemorrhages, Osler's nodules;
- focal or non-specific neurological symptoms;
- pulmonary emboli / infiltrates (right-sided IE);
- peripheral abscesses (kidneys, liver, spine) of unknown etiology.

According to modern criteria, a positive result of a microbiological blood test is a key moment in the diagnosis of IE, and data on the sensitivity of microorganisms to antimicrobial drugs determine the treatment tactics and prognosis of the disease.

Microbiological diagnosis of IE can be represented as an algorithm (Fig. 1).

III. IMAGING TECHNIQUESOF INFECTIVE ENDOCARDITIS

In order to avoid overuse of echocardiography, the decision to conduct or refuse an echocardiographic study should take into account the pretest probability of the disease.

Transthoracic echocardiography (TTE) should be performed first in all cases, as it is a non-invasive method that provides useful information for both diagnosis and assessment of the severity of IE. Transoesophageal echocardiography (TEE) should also be performed in most patients with suspected IE due to better image quality and better sensitivity, especially for diagnosing perivalvular disease. The only situation in which TTE can be considered sufficient is in the case of a qualitative negative TTE associated with a low level of clinical suspicion. (Fig. 2).

Knowledge of the anatomical features of IE is fundamental for a better understanding, analysis and description of the results of echocardiography [2]. Anatomically, IE is characterized by a combination of vegetations, destructive damages, and abscess formation.

Vegetations are usually attached to the valvular structure from the low pressure side, but can be located anywhere on the components of the valvular and subvalvular apparatus, as well as on the parietal endocardium of the chambers of the heart or ascending aorta. Large and mobile vegetations are prone to embolism and less often to valvular or prosthetic obstruction.

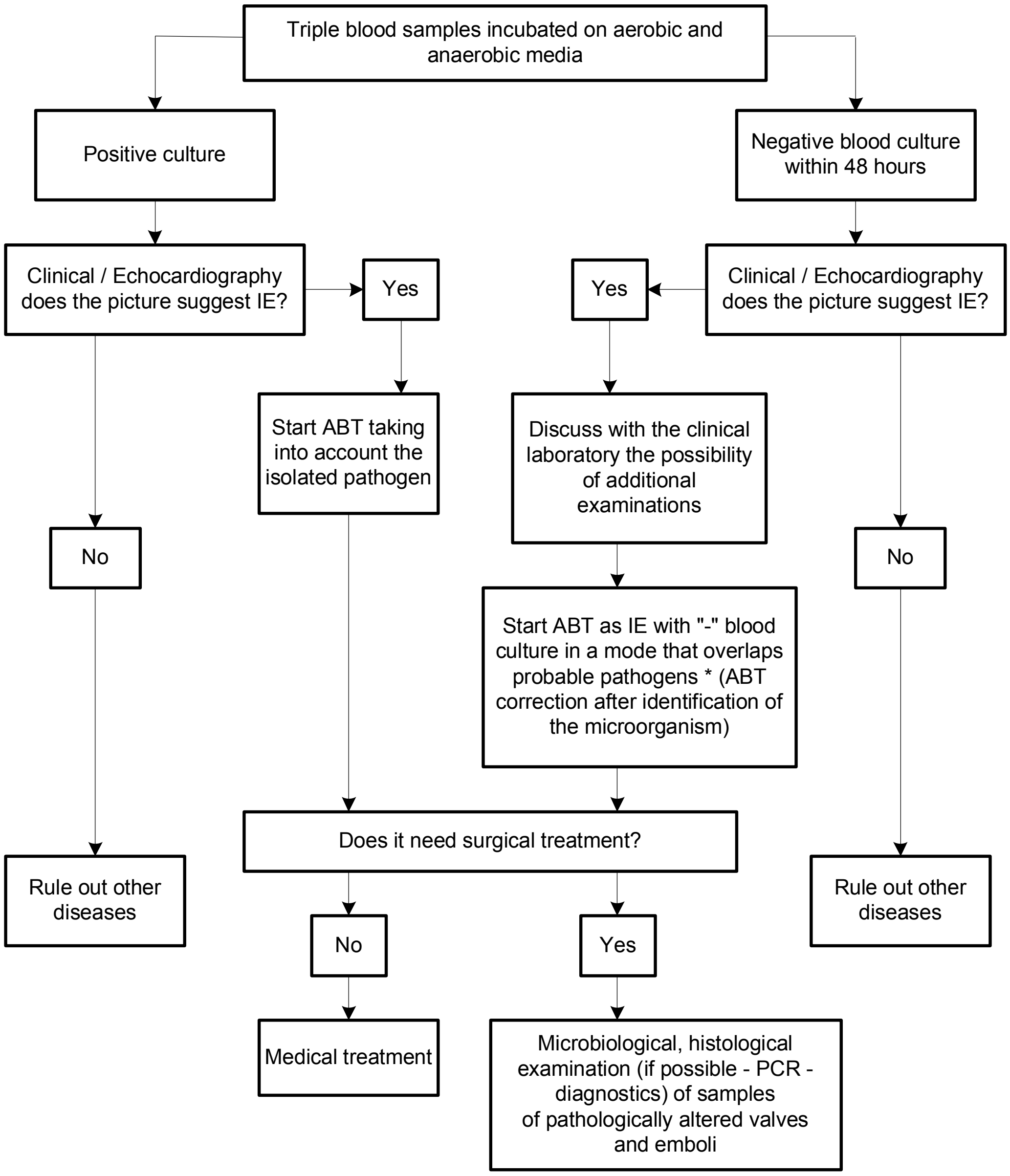

Fig. 1. Microbiological diagnosis of IE with positive and negative blood culture: IE is the infective endocarditis; ABT is the antibacterial therapy; PCR is the polymerase chain reaction

Destructive damages of the valves are very often associated with vegetations or can be observed separately. They can provoke valve aneurysm, perforation or prolapse, and rupture of the notochord or, less commonly, papillary muscle. The usual end effects of these damages are severe valvular regurgitation and heart failure.

The third main anatomical feature of IE is abscess formation. Abscesses are more common in aortic and prosthetic valve IE and may be complicated by pseudoaneurysm or fistulization.

These three anatomical features are often present together and must be carefully described on echocardiography.

The main echographic criteria for IE are vegetation, abscess, and new dehiscence of a prosthetic valve.

Vegetation is a hallmark of IE lesions. Typically, the vegetation is an oscillating mass attached to a valvular structure, with motion independent of valve motion. However, vegetations can also be non-fluctuating masses with atypical arrangements. The sensitivity of TTE for diagnosing vegetations is about 75%, but may be reduced in low echogenicity, very small vegetations, and in IE involving intracardiac devices or prostheses. Transesophageal echocardiography increases the sensitivity of TTE to approximately 85–90% for diagnosing vegetations, while the specificity of TTE and TEE is over 90% [2].

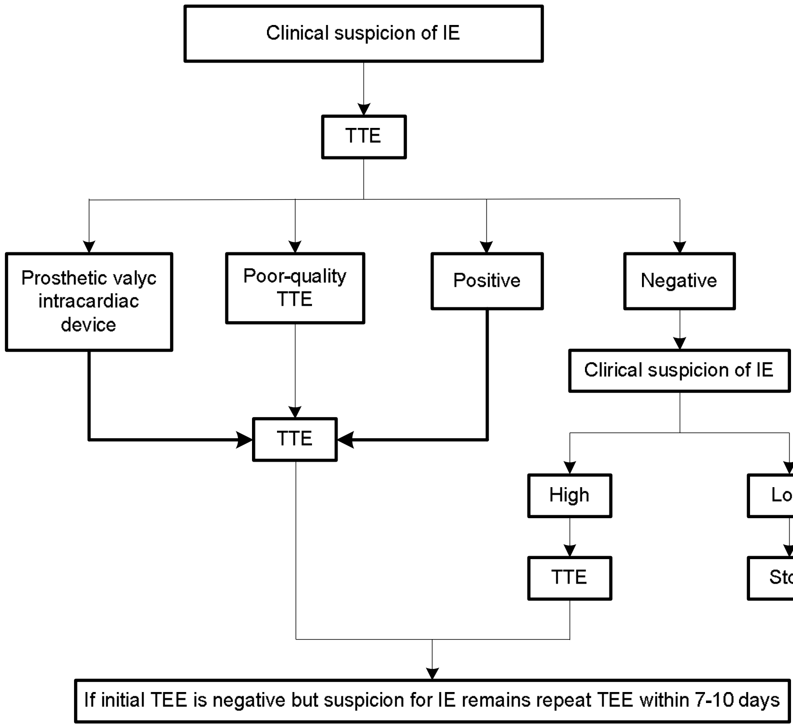

Fig. 2. Algorithm showing the role of echocardiography in the diagnosis and evaluation of infective endocarditis (adapted from Habib et al. [1] with permission). IE, infective endocarditis; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography

The second important echocardiographic criterion for endocarditis is the presence of a perivalvular abscess [2]. Abscesses are more common in aortic valve IE and usually involve mitral-aortic intervular fibrosis [3]. They are also more common in prosthetic valve IE. The abscess is usually a perivalvular area with reduced echogenic density, within which no color flow is detected. Diagnosis is simple in the presence of free space in the aortic root, but can be much more difficult in the early stages of the disease, when only thickening of the aortic root is observed [2]. The sensitivity of TTE for diagnosing abscesses is about 50% compared to 90% for TEE [4]. Therefore, TEE should be performed in all cases of aortic valve IE and when an abscess is suspected [4]. However, small anterior abscesses are sometimes difficult to diagnose with TEE and are best assessed with TTE. Therefore, both TTE and TEE are mandatory when perivalvular disease is suspected.

Echocardiography evaluates the number, size, shape, location, echogenicity, and mobility of vegetations [5] – [10]. Echocardiography is useful in predicting the risk of embolism and therefore plays a key role in identifying a subgroup of patients who may benefit from early surgical intervention to avoid embolism [6] – [12]. Several echocardiographic features of vegetations are associated with an increased risk of embolism. Vegetation size and mobility are powerful echocardiographic predictors of new embolic events [6]. Patients with vegetations larger than 10 mm are at higher risk of embolism [2]. This risk is even higher in patients with very large (>15 mm) and mobile vegetations [5], [6], [8]. Thus, careful measurement of maximum vegetation size at the time of diagnosis and during follow-up is strongly recommended as part of risk stratification. At the same time, embolisms occur more often in patients with vegetations located on the mitral valve (in particular, on the anterior leaflet of the mitral valve), as well as with an increase or decrease in the size of the vegetation on the background of antibiotic therapy [13], [7] – [9]. However, the possibilities of echocardiography for predicting the individual risk of embolism in patients remain limited [1], [14]. In fact, echocardiographic findings are not the only predictors of embolism.

In connection with the above, new imaging modalities, in addition to echocardiography, are now part of the diagnostic study of endocarditis [19]. These modalities include computed tomography (CT), ^{18}F-fluorodeoxyglucose positron emission tomography / low dose CT (FDG-PET/CT), and scintigraphy leukocytes with single photon emission computed tomography / low-dose CT.

Echocardiography, FDG-PET/CT, and multidetector CT angiography (MDCTA) with electrocardiogram (ECG) provide additional diagnostic information for suspected endocarditis / device infection. Accuracy of these methods was compared directly in a subset of patients referred to all of these imaging modalities [15].

As a result, echocardiography showed better results in the evaluation of vegetations, morphological abnormalities/valve dehiscence, septal defects, and fistula formation. MDCTA has performed best in the evaluation of abscesses and ventricular assist device infection. FDG-PET/CT showed the best results in assessing cardiac device infection, extracardiac infectious foci, and alternative diagnoses [15].

IV. STRUCTURE OF THE INTELLIGENT MEDICAL DIAGNOSTIC SYSTEM OF HEART VALVES

The structural diagram of the intelligent diagnostic system (IDS) is presented in Fig. 3 [16].

Information from the patient enters the system through the interface. Video images in digital form enter the filtering and geometric distortion removal units to eliminate the impact of noise. After that, the video image is sent to the abnormal area selection unit, which. as will be explained in the next subsections, implemented on the basis of a convolutional neural network. Evaluation of the signs that determine the presence of infectious endocarditis and the degree of its threat based on the detection of the amount, size, shape, location, echogenicity and mobility of vegetations according to the results of TTE, TEE and other methods is performed in the abnormal area evaluation unit.

Then the parameters of the signs obtained from the image analysis are compared with the normal state of the organ under investigation and with the pathological changes found in the database. It stores examination data and typical signs of diseases pre-formed using the statistical processing unit. This block interacts with the decision support block and creation of medical documents. On the basis of the data obtained from the block of information on the set of pathogenetic factors, the block of multifactor analysis allows you to draw up regression equations for them. Next, with the help of decision rules, a recommended solution is formed from the block of the same name.

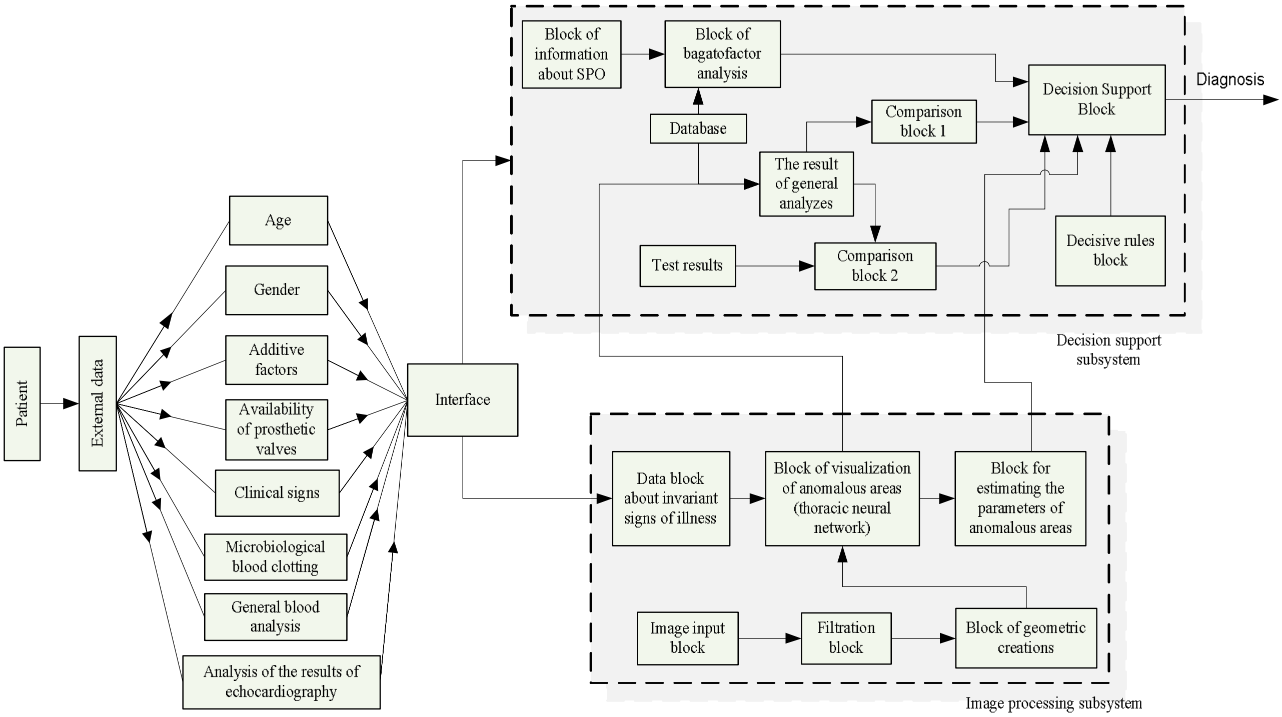

Fig. 3. Flowchart of smart diagnostics

The block of decision-making and creation of medical documents forms and displays special data on the monitor in a form convenient for the doctor, as well as evaluates their informational reliability and gives recommendations to the doctor for making a diagnosis, taking into account the factors affecting the disease.

Medical image segmentation aims to make anatomical or pathological structures changes in more clear in images; it often plays a key role in computer-aided diagnosis and smart medicine due to the great improvement in diagnostic efficiency and accuracy.

The goals of segmentation of medical images are to make changes in anatomical or pathological structures more distinct in the images; it often plays a key role in computer diagnostics and "smart medicine" by greatly improving the efficiency and accuracy of diagnostics.

To help clinicians make an accurate diagnosis, it is necessary to segment some important objects in medical images and extract features from the segmented areas. Early medical approaches to image segmentation often depend on edge detection, pattern matching techniques, statistical shape models, active contours, machine learning, etc.

Convolutional neural networks (CNNs) successfully achieve hierarchical feature representation of images, and thus become the hottest research topic in image processing and computer vision. As CNNs used for feature learning are insensitive to image noise, blur, contrast, etc., they provide excellent segmentation results for medical images.

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Semantic segmentation is the division of an image into several "related" parts, but without any attempt to understand what these parts represent. On the other hand, "semantic segmentation" attempts to break up an image into semantically meaningful parts, and classify each part into one of predefined classes. This is a form of pixel-level prediction because each pixel in an image is classified according to a category [17].

Thus, the following task is posed. For TTE and / or TEE echocardiograms of patient X_i where $X_i \in R^{n\times n}$ is the image matrix, define the label $y \in \{0, 1, 2, 3\}$, where "0" means no vegetation on the images, and "1, 2, 3" – presence and corresponding degrees of activity (size) (high, medium and low).

It is proposed to carry out the main segmentation processing of echocardiograms by an ensemble of deep convolutional neural networks focused on medical data.

V. SOLUTION OF THE SEGMENTATION PROBLEM

To carry out segmentation and create a classifier, it is proposed to use an ensemble approach with three medium-sized convolutional neural networks (the number of weights is less than 40 million). Ensembling involves the parallel use of several models with subsequent aggregation of the obtained independent results.

Each convolutional model must have a different topology and perform its own unique transformations to maximize diversity. The use of three networks is the minimum for majoritarian voting, since in this case two networks can already create a majority, thus creating a balance of accuracy (since the three networks will complement and refine each other's values) and calculation speed (using only 3 networks).

Each convolutional model must have a different topology and perform its own unique transformations to maximize diversity.

This paper proposes the use of the following modern segmenter architectures, which are generally designed specifically for medical data: DeepLabv3+, ResUNet++, NanoNet. These networks were successfully applied by the authors of this article in the construction of an intelligent medical diagnostic system for determining the degree of activity of pulmonary tuberculosis [18]. Each model has a different topology, although most follow the encoder-decoder approach. The use of different types of transformations (ASPP, SE, residual), as well as different types of pre-trained backbone networks (ResNet50, MobileNetV2) allow us to maximize the variety of features obtained by these networks.

Each network in the ensemble works in parallel and independently, giving the output matrix $Y \in \{y \in \mathbb{R} | 0 \le y \le 1\}^{n\times n}$, where each element is the probability of vegetation in the pixel. If the value is less than 0.5, then the probability of vegetation is less than 50%.

Next, the *maximum* function is used to aggregate all masks. The value of each pixel of the aggregated matrix is determined by the following formula:

$$y_{ij} = \max_{k\in N} y_{ij}^{(k)},$$

where *i, j* are the coordinates of the matrix element; *N* is the number of segmenters; $y_{ij}^{(k)}$ is the value *i*, *j* of the element of the output matrix of the *k*th segmentator.

After obtaining the aggregated matrix, a threshold with a value of 0.5 is applied (that is, the probability that there is vegetation in the pixel is greater than 50%) to binarize it. Thus, the resulting matrix is obtained $Y \in \{0,1\}^{n\times n}$, where "0" means the absence of vegetation in a given image pixel, and "1" means the presence. The algorithm for calculating the individual contribution of each network to the ensemble is given in [18] and is not considered here.

To solve the binary classification problem, MobileNetV2 binary classifiers were used. Determination of the degree of disease activity is made on the basis of an analysis of the size of the vegetation and their echogenicity.

VI. Experimental Results

The following metrics were used to test the accuracy of binary classification models:

1) Accuracy;
2) Precision and Recall;
3) F1 and F2 scores.

The following metrics were used to test the accuracy of segmentation models, cleaning and ensemble algorithms:

1) Mean intersection over union (mIoU);
2) Dice score;
3) Precision and Recall;
4) F1 and F2 scores.

The overall accuracy of the classification solution (determining the level of vegetation growth activity) was more than 90%. In the context of patients, this means only one misclassified case, but within adjacent levels (low-medium).

VII. Conclusion

A new approach is proposed in the diagnosis and determination of the level of threat to the patient's life in the case of infective endocarditis. The proposed approach is based on the use of artificial intelligence methods, which makes it possible to identify vegetations, determine their size and echogenicity. This will prevent the occurrence of an embolism.

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Sineglazov Victor. ORCID 0000-0002-3297-9060.
Doctor of Engineering Science. Professor. Head of the Department.
Aviation Computer-Integrated Complexes Department, Faculty of Air Navigation Electronics and Telecommunications, National Aviation University, Kyiv, Ukraine.
Education: Kyiv Polytechnic Institute, Kyiv, Ukraine, (1973).
Research area: Air Navigation, Air Traffic Control, Identification of Complex Systems, Wind/Solar power plant, artificial intelligence.
Publications: more than 700 papers.
E-mail: svm@nau.edu.ua

Chumachenko Olena. ORCID 0000-0003-3006-7460.
Doctor of Engineering Science. Professor. Head of the Department.
Department of Artificial Intelligence, Faculty of Informatics and Computer Science, National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute", Kyiv, Ukraine.
Research area: artificial neural networks, artificial intelligence
Publications: more than 120 papers.
E-mail: eliranvik@gmail.com

Kolomoiets Serhii. PhD Student. ORCID 0000-0003-3741-4517.
Department of Information Systems, Faculty of Informatics and Computer Science, National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute," Kyiv, Ukraine.
Education: National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute", Kyiv, Ukraine.
Research interests: artificial neural networks, artificial intelligence.
Publications: 1.
E-mail: serhii.o.kolomoiets@ukr.net

В. М. Синєглазов, О. І. Чумаченко, С. О. Коломоєць. Визначення характеристик інфекційного ендокардиту на основі інтелектуальної обробки ехографічних зображень

У роботі представлено патогенетичні фактори розвитку інфекційного ендокардиту та визначено його предиктори. Показано необхідність ехографічного дослідження пов'язаного з пошуком анатомічних характеристик інфекційного ендокардиту: вегетації, деструктивних уражень (аневризми клапана, перфорація або пролапс, тощо), наявність абсцесів, у разі протеза характерною особливістю може бути нова розбіжність протеза клапана. Представлена класифікація методів дослідження, яка включає класичні підходи ехокардіографії (трансторакальна, чреспищеводна) та нові мультидетекторну комп'ютерну томографічну ангіографію та позитронно-емісійну томографію з ^{18}F-фтордезоксиглюкозою та визначена в різних випадках. Розроблено структурну схему інтелектуальної діагностичної системи інфекційного ендокардиту. Для обробки отриманих зображень з метою діагностики та визначення геометричних розмірів, форм, кількості, розташування, характеристик інфекційного ендокардиту запропоновано використовувати згорткові нейронні мережі, які дозволяють вирішувати задачу сегментації зображень.

Ключові слова: ехокардіографія; ендокардит; хвороба клапана; інтелектуальна обробка; ехографічні зображення.

Синєглазов Віктор Михайлович. ORCID 0000-0002-3297-9060.
Доктор технічних наук. Професор. Завідувач кафедри.
Кафедра авіаційних комп'ютерно-інтегрованих комплексів, Факультет аеронавігації електроніки і телекомунікацій, Національний авіаційний університет, Київ, Україна.
Освіта: Київський політехнічний інститут, Київ, Україна, (1973).
Напрям наукової діяльності: аеронавігація, управління повітряним рухом, ідентифікація складних систем, вітроенергетичні установки, штучний інтелект.
Кількість публікацій: більше 700 наукових робіт.
E-mail: svm@nau.edu.ua

Чумаченко Олена Іллівна. ORCID 0000-0003-3006-7460. Доктор технічних наук. Професор. Завідувачка кафедри.
Кафедра штучного інтелекту, Факультет інформатики та обчислювальної техніки, Національний технічний університет України «Київський Політехнічний Інститут імені Ігоря Сікорського», Київ, Україна.
Кількість публікацій: більше 120 наукових робіт.
Напрям наукової діяльності: штучні нейронні мережі, штучний інтелект.
E-mail: eliranvik@gmail.com

Коломоєць Сергій Олексійович. Аспірант. ORCID 0000-0003-3741-4517.
Кафедра інформаційних систем та технологій, Факультет інформатики та обчислювальної техніки, Національний технічний університет України «Київський Політехнічний Інститут імені Ігоря Сікорського», Київ, Україна.
Кількість публікацій: 1.
Напрям наукової діяльності: штучні нейронні мережі, штучний інтелект.
E-mail: serhii.o.kolomoiets@ukr.net