UNIVERSITY OF PECS
FACULTY OF HEALTH SCIENCES

DOCTORAL SCHOOL OF HEALTH SCIENCES

DIFFERENTIAL DIAGNOSIS AND MANAGEMENT OF PATIENT PATHWAYS ON THE ACUTE CARDIOVASCULAR DISEASES- FOCUSING ON THE PULMONARY EMBOLISM AND NSTEMI

Head of the Doctoral School: Prof. Dr. József Bódis

Programme leader: Prof. Dr. Gábor L. Kovács

Supervisor: Dr. Balázs Radnai

Doctoral (Ph.D.) thesis

Attila Pandur

Pécs, 2023

1. INTRODUCTION

The independent development of multidisciplinary emergency care and the appearance in the organization of care is the achievement of the past 50 years, so it is now an unquestionable actor and care organizing factor in the health care system. Cardiovascular diseases also play a leading role in mortality in Hungary. Based on the health status of the Hungarian population, Hungary ranks in the middle of the world, but it is one of the most disadvantaged countries in Europe. Cardiovascular events, acute coronary syndrome (ACS), stroke, and pulmonary embolism (PE) should be highlighted. High workloads in emergency departments are a growing concern worldwide, meaning patients stay longer in the department, negatively affecting the quality of care and timely access to health care. The clinical symptoms of the two cardiovascular diseases discussed in the dissertation can be very similar, which makes differential diagnosis between acute coronary syndrome and pulmonary embolism difficult. In emergency care, patients suffering from the two pathologies present with varied clinical manifestations and non-specific symptoms, and cardiac biomarkers can be elevated in both diseases. In our research, we analyzed the differential diagnosis and decision-making situations of two disease processes with varied clinical symptoms and a high time factor, in which survival estimation is essential for early, quick decision-making.

2. AIMS OF THE THESIS

Objectives related to pulmonary embolism:

1. Our goal is to assess the risk factors of confirmed PE patients in the Hungarian population to compare them with the data available in the international literature.
2. In order to facilitate the differential diagnosis, we aimed to evaluate the main complaints of PE patients presenting to the emergency department and their role in the field of differential diagnosis.
3. Since most symptoms do not have sufficient predictability to confirm PE, the importance of using score systems is increased. Therefore, we set as an additional goal the examination of the predictability of the score systems available in the international literature in the domestic population, which can be realized with a posteriori score calculation.
4. In this context, we are trying to improve the predictive values of the two risk assessment score systems (Wells score, modified Geneva score) proposed by the ESC 2019 guideline to propose to modify the examined factors.

5. The predictability of risk stratification score systems can be significantly increased by considering laboratory diagnostic findings. Based on this, we aim to examine the predictability of the age-correlated D-dimer assessment in the previously referenced clinical guideline published in 2019 on a domestic sample and, based on the results, make recommendations for its adaptation.

6. With the post-calculation of the clinical risk assessment score systems, we can compare scoring systems not routinely used in clinical practice, so we can make suggestions for increasing cost-effectiveness by using diagnostic tools more rationally.

7. Among the diagnostic tools available in the prehospital setting, we tried to find the role of electrocardiography in identifying the disease process by examining the diagnostic value of ECG changes, which is necessary to determine its predictive indicators.

8. The prognostic score systems help to consider the risk/benefit ratio and its validity during the decision about the intervention. Therefore, our goal is to determine the predictive indicators of the prognostic score systems (PESI, sPESI, HESTIA) through the follow-up examination of confirmed PE patients to objectify the extent to which it can contribute to clinical decision-making.

9. Finally, by examining the HESTIA criteria available in the international literature on the Hungarian sample, we aim to prove its role in the decision on early discharge, thus proposing its adaptation in Hungary.

NSTEMI-related objectives:

1. In the case of coronary occlusion, reperfusion as soon as possible requires the minimization of prehospital and hospital delays. In order to do this, we propose to minimize the delay with the post-calculation of the clinical risk estimation score systems, for which we are looking for the most suitable on-site risk stratification tool, including detectable ECG deviations. For this purpose, by comparing the predictability and the examined elements of the post-calculated score systems (not examined by the provider during diagnosis), we try to filter out individual factors that underestimate or overestimate the clinical probability.

2. The test's predictive indicators are poor in the case of a moderate increase in the troponin plasma level (grey zone). In order to increase this, repeating the examination is justified, which, as we saw earlier, prolongs the diagnosis by hours. We aim to investigate how the delay occurring due to repeating the initial gray zone troponin

value can be reduced. To this end, we are investigating which clinical risk assessment score system can be used to reduce the time lost due to the currently valid 0/3 hour troponin sampling.

3. Another "leg" of AMI diagnostics is the analysis of ECG deviations. During our tests aimed at improving the predictability of electrocardiography, we examine the ECG registers of recent NSTEMI cases in the selected emergency department, looking for a deviation or characteristic that can help to increase the diagnostic value of the test in case of suspected NSTEMI.

3. TEST MATERIALS AND METHODS

The research was a multicenter, quantitative longitudinal study with retrospective elements. In Hungary, we selected five emergency departments with different levels of progression. (Pécs, Szekszárd, Dunaújváros, Zalaegerszeg, Győr) We selected our target group from the patients admitted to the emergency department between 2011 and 2020. Target group: We examined patients admitted to the emergency department with clinical symptoms and complaints that raise the suspicion of pulmonary embolism and/or NSTEMI. Inclusion criteria were defined as Troponin and/or D-dimer sampling based on the evaluation of the chief complaint and symptoms in the emergency department during the examined period or that a BNO code was recorded in the context of PE/NSTEMI in the discharge diagnosis. Patients for whom the clinical risk assessment score systems could not be calculated retrospectively as a means of differential diagnosis were excluded. Furthermore, there was no description available in the documentation during the ECG examination, or we could not perform a 30, 60, 90-day and 1-year follow-up in the documentation, focusing on early discharge. In the examined period, we conducted sub-researches to evaluate or modify a risk estimation score system, during which sub-samples were formed. To study our objectives related to pulmonary embolism and NSTEMI, we formed a total of 3 different subsamples as follows:

➢ PE_{R1}: We performed a descriptive analysis of confirmed PE cases (1510 people) from the 10-year patient records of the five emergency departments in order to compare the international occurrence of predisposing factors and to model the modification of the subjective Wells score. In this sub-sample, from the 10-year time interval, all patients in whom PE BNO was recorded as the diagnosis at discharge from the hospital and who visited the emergency department before that were included. We performed a retrospective analysis to evaluate the predisposing factors, leading complaints, and symptoms among these patients, and we performed modeling to improve the predictive indicators of the Wells score.

➢ PE_{R2}: The training of these subsamples consisted of 652 patients from the patient material of an emergency department. As a target group, we examined patients who came to the emergency department with symptoms or complaints suspected of PE. In our subsample, we tested the modified version of the two score systems proposed by the ESC (Wells score and modified Geneva score) combined with the chief complaint and the predictive indicators of clinical risk

assessment score systems, which are less known in Hungarian emergency care, were retrospectively calculated with retrospective data analysis.

➢ PE$_{R3}$: We were able to test the possibilities of home discharge of confirmed PE patients on a sub-sample with a smaller number of items (N=405 people) of patients of a central hospital in the period 2015-2018. In the case of this sub-sample, the target group was patients discharged from the hospital with the BNO code pulmonary embolism and who visited the emergency department. We subsequently calculated the three prognostic score systems.

➢ NSTEMI$_{R1}$: We tested a risk assessment score system (HEART-score) standard in international care, modeling how much benefit patients can derive from early differential diagnosis using the scoring system. As a target group, we examined patients admitted to the emergency department with chest pain and/or equivalent complaints and symptoms. The research was a quantitative longitudinal study with retrospective elements, the first pilot element of a planned study with a more significant number of elements. After obtaining the necessary permits (FO/410/2019), we collected data in a county seat's emergency department. Time interval of the analyzed patient documentation: January 1, 2015-2018. August 31. As an inclusion criterion, we determined that NSTEMI BNO was recorded in at least one of the diagnoses of the patients treated in the emergency department. Those with incomplete documentation were excluded from our sample, so we could not calculate a risk estimate afterward.

➢ NSTEMI$_{R2}$: After randomization (Research Randomizer) from a database of 28,000 patients, we had the opportunity to perform an analysis in the emergency department of a central hospital for the early screening of the NSTEMI patient population for the joint evaluation of the Troponin and clinical risk assessment score systems. The target group was defined as having an initial Troponin value during the period under study. After validating the exclusion criteria, we examined 270 patients due to incomplete documentation. Coronary occlusion results were incomplete for 199 of these patients, so we were able to perform subsequent score calculations for a total of 71 patients.

➢ NSTEMI$_{R3}$: In a five-year time interval of the patient traffic of a central hospital, we analyzed the ECG curves of patients with a diagnosis of NSTEMI retrospectively and prospectively, in whom we also had findings of PCI at

follow-up (N=500 people). In order to determine the predictive indicators of characteristic ECG abnormalities in the case of NSTEMI, we also examined less common changes, such as the N-wave. In the case of our sub-sample, we formulated as an inclusion criterion that the patient visited the emergency department before recording the NSTEMI BNO code for discharge from the hospital. Cases where ECG analysis was incomplete, were excluded.

For each of our sub-samples, the data collection took place in the form of document analysis, during which we wanted to examine the patient's socio-demographic data, underlying diseases, medications they were taking, chief complaint, vital parameters, laboratory and imaging test results, time spent in hospital, elements of PE and NSTEMI clinical risk assessment score systems, ECG descriptions, to model early discharge of PE, complications during follow-up, death at 30, 60, 90 days, and 1-year survival. Patient documentation accessible through the IT systems of the selected hospitals served as a data source. Data processing was carried out using IBM SPSS version 26.0 statistical software. Descriptive statistics were prepared, as well as mathematical statistics for correlation and difference tests (Chi-square test, ANOVA, correlation calculation, T-test. The significance limit was established at $p \leq 0.05$, i.e., at a 95% confidence interval. Microsoft Excel (Office 365) and IBM SPSS 26.0 statistical software were used during the research. The necessary research permits were obtained for each hospital before the examination. Below are the identifiers of the research ethics permits: Szekszárd: FO/410/2019, Pécs, Zalaegerszeg, Dunaújváros: Research work authorized through the Regional Research Ethics Committee: PTE/72017/2018, Győr: 011484-1/2019.

4. ANALYSIS AND RESULTS

The top complaints among patients presenting to the emergency department with suspected pulmonary embolisms are extraordinarily diverse and widespread. This draws attention to the importance of thorough diagnostic activity, during which the probability of diagnosis can be increased to the expected extent. These presentation complaints are presented in the following table.

Complaints	PE (1510 person)	Frequency of occurrence (%)
No complaints	91	6%
Chest pain	743	49,2%
Back pain	404	26,75%
Dyspnoea	884	58,5%
Weakness	236	15,62%

Syncope	155	10,2%
Abdominal pain	48	3%
Dizziness	32	2%
Cough	235	15,5%
Hemoptysis	91	6%
Chest AND back pain AND shortness of breath	102	6,7%
Chest AND back pain	162	10,7%
Chest AND shortness of breath	471	31,2 %

With the help of retrospective data collection on our PE_{R1} sample, we calculated the predictive indicators of the two score systems recommended for pulmonary embolism and two less familiar but reliable score systems used in international care, summarized in the table below.

Score systems	Sensitivity	Specificity	PPV	NPV
Wells-score	85,7 %	78 %	87 %	96 %
Revised Geneva-score	84 %	89,7 %	80,1 %	90,5 %
PERC	82,1%	57,6%	61,0%	80,0%
4PEPS	92,6%	82,3%	47,7%	98,4%

Examining international literature, we did not find any research that dealt with the possibilities of improving the predictive indicators of validated clinical risk assessment score systems for effective recognition in emergency care. We analyzed the leading complaints and, based on the frequency of occurrence, supplemented the two risk stratification score systems proposed by the ESC with leading complaints. During subsequent document analysis, we calculated the predictive indicators of each PE clinical risk assessment score system based on the definitive diagnosis. The following tables show the predictive indicators calculated for the tested score systems and their modified versions.

Score systems	Sensitivity	Specificity	PPV	NPV
Wells-score	76,3%	95,3%	92,9%	83,3%
Revised-Wells	84,9%	85,3%	82,3%	87,5%
Geneva-score	79,7%	53,2%	57,9%	76,5%
Revised-Geneva	82,1%	57,6%	61,0%	80 %
PERC	92,1%	24,1%	49,4%	79,1%

During the examination of score systems modified by the implementation of the leading complaint, we verified on our sample that they could be used with higher predictability to rule out PE. In the following, we attempted (PE_{R1}) on the entire sample to modify the original class intervals and weight values (scores) assigned to the symptoms of the Wells score

recommended by the guideline to improve the predictive indicators. The fundamental difference between the two score systems is the existence of the subjective factor. For this reason, we analyzed how the predictive indicators of the Wells score change without the subjective point value.

subjective point 3			
	low	intermediate	high
Specificity	96,39%	48,50%	50%
Sensitivity	46,42%	91,90%	98,27%
PPV	30,90%	66,28%	81,42%
NPV	98,10%	84,50%	92,85%

subjective point 2			
	low	intermediate	high
Specificity	96,39%	20,50%	50%
Sensitivity	46,42%	91,68%	98,60%
PPV	30,90%	67,00%	78,02%
NPV	98,10%	58,37%	95,23%

subjective point 1,5			
	low	intermediate	high
Specificity	-	-	50%
Sensitivity	-	-	95,80%
PPV	-	-	71,00%
NPV	-	-	90,00%

subjective point 1			
	low	intermediate	high
Specificity	-	-	50%
Sensitivity	-	-	91,60%
PPV	-	-	70,90%
NPV	-	-	81,81%

The Daniel ECG-score, published in the last decades and has increasingly better predictive indicators after further modifications, was calculated retrospectively based on the retrospective data on a sample of 1,510 people. The retrospectively calculated predictive indicators of the Daniel ECG score in the patient population of the five emergency departments we examined were as follows:

Sensitivity	Specificity	PPV	NPV
87,7%	51,0%	48,7%	92,9%

Predictive indicators of Daniel's ECG score in our domestic PE suspect sample

Based on international research, a validated algorithm has been created in the last 10 years to facilitate the safe home treatment of patients with pulmonary embolisms. Using the three

validated prognostic score systems proposed based on the pulmonary embolism guideline published in 2019 by the European Society of Cardiology, we examined how many patients could be discharged safely and without complications from the hospital as soon as possible in the patient population of an emergency department. We also examined the effectiveness of the three prognostic score systems on subsamples formed by age. We found no difference when examining the age group over and under 50 (p=0.832). Based on international guidelines, the prognostic score system is safe if no severe complications and/or death occur in connection with VTE within 30 days. We supplemented this by examining the one-year mortality indicators for all three score systems. We considered the prognostic score safe and effective if there was no rehospitalization within 30 days and no death in connection with VTE within 1 year. The table below summarizes the predictive indicators of the three prognostic score systems.

	Sensitivity	NPV	PPV	Specificity
PESI	91%	98%	32%	57%
sPESI	100%	100%	20%	30%
HESTIA	100%	100%	18%	30%

Predictive values of prognostic score systems

Our research on the NSTEMI patient population focused on early detection, clinical decision-making, and the decision-supporting role of the ECG.

1. We tested the HEART-score, the most usable score system according to international literature, on a sample of patients from a rural emergency department.

2. In the emergency department of a central hospital with a patient population of 28,000, after randomization, we determined the predictive indicators of clinical risk assessment score systems in order to identify the high-risk NSTEMI patient population early.

3. We performed an ECG evaluation among patients diagnosed with NSTEMI in the emergency department.

In the following, we present our retrospective, quantitative study of one subsample (NSTEMI$_{R1}$), which we conducted in the emergency department of a rural county seat among patients with a BNO code related to a heart attack. Our research aimed to examine the time and care effects of the HEART score as a risk stratification tool for patients with myocardial injury. The elements of the HEART score include the examination of the ECG, so we examined whether there is a correlation between the presence of an ECG abnormality and admission to the cardiology center. In the case of patients whose ECG records showed abnormal changes (n=178), the average SBO-PCI time was 102.69 minutes. In the cases

indicated as having no ECG abnormalities (n=43), the average time was 145.4 minutes (p=0.001). Among patients with detectable ECG abnormalities suggestive of ACS (n=220), the death rate was 15.9% (n=35), while among cases without ECG abnormalities (n=57), 12.3% -os (n=7), the death rate (p=0.326). During the post-risk stratification, we tested the HEART-score on a Hungarian sample, looking for a correlation between the post-calculated HEART-score value and the SBO-PCI time. By comparing the HEART-score value of the examined emergency department patients (n=221) with the SBO-PCI time, we concluded that there is a significant correlation between the two variables (p=0.005 F=-0.190). Therefore, patients with a higher post-calculated HEART score underwent PCI more quickly (that is, the SBO-PCI time was shorter in their case) than those with a lower score (below 5 points). From a database of 28,000 people, we had the opportunity to examine 300 cases and subsequently perform a score calculation randomly. The initial troponin test results were available for early detection. (NSTEMI$_{R2}$) We analyzed the data of 300 patients, all of whom had at least one troponin result from multiple times the expected value.

During the retrospective data collection, we determined the predictive indicators of 8 score systems suitable for the differential diagnosis of NSTEMI and/or chest pain in our domestic sample.

In the following table, we have summarized the predictive indicators of the eight score systems calculated retrospectively on our sample.

Score system	Sensitivity	Specificity	NPV	PPV
Action ICU	92%	3%	25%	49%
PRO-ACS	42%	80%	57%	68%
HEART	94%	3%	93%	50%
PURSUIT	39%	80%	56%	67%
TIMI	92%	26%	75%	56%
C-ACS	25%	77%	50%	53%
GRACE	83%	40%	70%	59%
FRISC	6%	94%	49%	50%

Predictive indicators of clinical risk assessment score systems were calculated retrospectively on the suspected NSTEMI patient population.

We examined the ECG curves of patients diagnosed with NSTEMI (NSTEMIR3) during five years of patient traffic in a central hospital. In the following table, we have summarized the ECG changes that we experienced during the ECG analysis.

	Frequency of occurrence (pcs)	verified occlusion (p-value)
Normal ECG	124	0,001
normal ST	317	0,147
ST depression	291	0,017
Normal T wave	314	0,961
Negative T wave	157	0,990
Coronary T wave	7	0,003
Q wave	102	0,331
PQ interval	156+-30 ms	0,759
QRS interval	103+-21ms	0,336
QTC time	437+-35 ms	0,329
Axle position		
normal	412	0,287
left deviation	196	
right deviation	12	
LBBB	18	0,05

ECG changes in patients with suspected NSTEMI in the emergency department

In our study, we attempted to look for deviations, the recognition of which could facilitate the early identification of high-risk NSTEMI patients. We present our results related to a less well-known wave in the following.

N wave

An international publication defined the N-wave as follows: "A notch or deflection in the ventricular complex of the ECG, the height of which exceeds 0.2 mV (this height is measured relative to the PR segment). The N wave seen in the ventricular complex is an abnormal waveform, which is a delayed activation wave of the basal region of the left ventricle, which can be traced back to the left circumflex artery (LCX). We identified the mentioned wave in the ECG findings of 66 patients. The following predictive values were obtained in the case of N-wave and ST-depression.
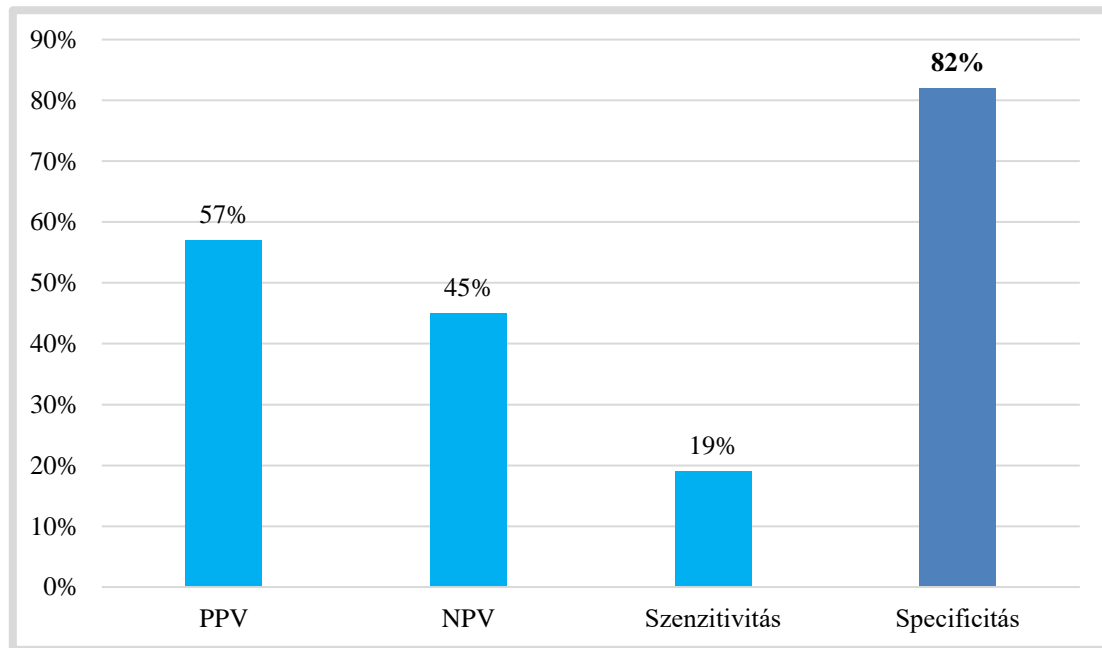
Common predictive indicators of N-wave and ST-depression

The statement "Time is the heart muscle, the heart muscle is life" captures the need to diagnose cardiovascular pathologies rapidly. Symptoms of pulmonary embolism and acute myocardial infarction may be similar, including sudden onset of dyspnea, chest pain, collapse, syncope, and palpitations. Based on the results of our research, clinical risk assessment score systems play an essential role in choosing a diagnostic strategy. In the case of pulmonary embolism, the predictive indicators of the eight score systems calculated retrospectively are no worse than the predictive indicators available in the international literature. Taking this as a basis, it can be stated that, similarly to international practice, it can be safely used in decision-making in our country. In the case of the 4PEPS score published in 2021, we found better predictive indicators in our sample than during the initial validation international research. We attempted to improve the predictive indicators of the two clinical risk assessment score systems recommended by the guideline. In the international literature, we did not find any study that examines the joint evaluation of score systems with leading

complaints. Therefore, after determining the odds ratios for the two scores, we weighted the leading complaints by assigning scores, thereby improving the predictive indicators of the two scores. The trend, which can be filtered out of our results, provides an opportunity for the predictive indicators of the scoring system modified with the two leading complaints to improve when modeled with a higher number of elements. According to the post-calculated predictive indicators of the score systems used in the differential diagnosis of NSTEMI and chest pain, the specificity of the FRISC score in our sample is 94%, and that of PRO-ACS and PURSUIT is 80%. Based on our research, these three scores, mostly the FRISC, can be excellent rule-out scores thanks to their 94% specificity. If we look at the examined factors, relatively few variables are required, which can be quickly measured in emergency care, thus reducing the possible waiting time. The sensitivity of the HEART score was the highest in our sample. We calculated a result of 94% during the subsequent score calculation. In conclusion, the HEART score provides an appropriate tool for EDs in making disposition decisions in patients presenting to the ED with chest pain or ACS-equivalent complaints. The modified form of the HEART score may be suitable for prehospital decision-making. In the case of the two pathologies, the sensitivity indicators of the ECG test do not allow the test to be used independently during the early identification of disease processes. In the case of pulmonary embolism, we examined the predictive indicators of the Daniel ECG score with subsequent calculation. The predictive indicators determined from the samples fell short of the values published by Vereckei et al. in 2020, in which the predictive indicators of the score make it suitable for everyday use in prehospital care without laboratory diagnostics for patient path management (predictive values obtained during our research: sensitivity: 98 %, NPV: 98%, PPV 77.3%, specificity: 69%). Our research results show that both HESTIA criteria (100% NPV, 100% sensitivity) and PESI (98% NPV, 91% sensitivity) or sPESI (100% NPV, 100% sensitivity) can reliably identify those patients who have a low risk of death. Our results are strengthened by the fact that similar predictive values can also be found in the international literature.

5. NOVEL FINDINGS AND PRACTICAL APPLICATIONS

The results of our research, presented by the objectives formulated for the problem statements presented in the dissertation, contain several new results that prove to be helpful in the differential diagnosis of pulmonary embolism and NSTEMI among acute cardiovascular pathologies, enabling the creation of a chest pain diagnostic and decision-making support software that can facilitate early diagnosis. The results are summarized below:

- ✓ This research in the differential diagnosis is the research with the most significant number of elements in Hungary.
- ✓ We retrospectively calculated 16 clinical risk assessment score systems.
- ✓ In international and domestic care, we were among the first to improve the predictive indicators of the two score systems proposed by the ESC (Wells and modified Geneva score) with a weighted evaluation of the leading complaint.
- ✓ The age-correlated D-dimer was tested for the first time on a Hungarian sample, which helps to reduce the number and harmful effects of unnecessary imaging tests.
- ✓ The 4PEPS score published in international care was tested on a domestic sample and achieved better predictive indicators than in the international validation study.
- ✓ We created the possibility of evaluating the risk associated with the early discharge of confirmed PE patients by modeling all three prognostic score systems recommended by the ESC guideline on a domestic sample.
- ✓ With the results presented in our research, significant cost-effectiveness in domestic care can be achieved through earlier recognition, more conscious diagnostic activity, a more selectable and supported decision-making strategy, and a reduction in the number of days spent in the hospital.
- ✓ For the NSTEMI patient population, we tested and searched for new ECG abnormalities, such as the N wave, for the first time in a domestic sample.
- ✓ We proved that NSTEMI diagnosis could be improved by evaluating the combined presence of the N-wave and significant ST depression. Thus, shortening the patient pathway can reduce the total ischemic time.
- ✓ For the first time, we tested the less common score systems suitable for the differential diagnosis of chest pain in the Hungarian sample.
- ✓ In order to reduce the delay associated with the 0/3-hour laboratory diagnostic algorithm, the HEART-score, and initial Troponin predictive indicator are safe and effective in identifying high-risk patients.
- ✓ We have created a database that can form the basis for creating a chest pain differential diagnosis algorithm and software with the support of artificial intelligence.

6. SUGGESTIONS

In the past, the analytical and intuitive skills of clinical providers, thus empiricism, were of great importance since, compared to today's conditions, they had orders of magnitude fewer data at their disposal, for example, in the field of cardiovascular diseases. As a result, it was often necessary to wait for the patient's condition to change so that the appropriate diagnosis could be established based on its direction and progress. The doctor's experience and ability to analyze and synthesize played a considerable role. Medicine is developing and modernizing, but care costs are also increasing. Thanks to the data explosion, obtaining a fantastic amount of data about the patient during his care is now possible. Think of the development of imaging equipment and procedures or laboratory medicine. At the same time, errors in diagnosis still range between 10-15%. During our research, we investigated how to diagnose pulmonary embolism and NSTEMI in emergency care with sufficient accuracy, a high hit rate, and at the same time, quickly and cost-effectively. It is a current topic, as cardiovascular diseases are associated with high mortality in Hungary. In many countries, different risk stratification procedures are used to manage the care of patients presenting with chest pain. All the score systems we have examined and used in clinical practice are based on scientific evidence, which can be found in the international literature.

Examining a 10-year time interval, we analyzed the data of 3,510 patients in five emergency departments, examining them from several aspects and exploring the factors promoting differential diagnosis. We identified the risk factors, improved the predictive indicators of clinical risk assessment score systems, defined the role of ECG in managing the patient journey, formulated a proposal for faster diagnosis in the NSTEMI patient population, and prepared the implementation of the early discharge of confirmed PE patients. Several research questions emerged even during the research, to which we must find answers in the future. In the case of confirmed PE patients, it is more challenging to decide on immediate or early discharge and what kind of laboratory and imaging diagnosis can be performed for medium-risk confirmed pulmonary embolism patients without an underlying disease, which we will seek to answer in subsequent research. A further research task is to investigate why PCI intervention was not performed in high-risk patients based on the retrospectively calculated HEART score and whether clinical risk assessment score systems should be available in emergency care in a manner adapted to the use of artificial intelligence, which, with the help of decision tree models, would be suitable for demonstrating a benefit analysis. A unique solution for the early differential diagnosis of chest pain can also be developed in international care. For the future, we have set ourselves the goal of developing an artificial intelligence-based decision support system that, in the form of a web application, is trained on

the data provided to us, using the toolset of interpretable machine learning and explainable artificial intelligence (XAI), can help with a probability value for pulmonary embolization, as well as emergency diagnosis of the acute coronary syndrome, in addition, the developed system also provides an individual-level explanation of the model's outcome.

When evaluating healthcare procedures, we keep four things in mind: quality, effectiveness, safety, and efficiency. Our study revealed that risk assessment systems have all four properties. It was found that following the protocol properly could save money for the healthcare system. In addition to health-economic gains, patients can also benefit from our research results. With our research, we also highlighted the critical fact that the early discharge of confirmed PE patients could increase patient satisfaction and the trend in which home care will play a significant role by supporting and promoting prevention with intelligent devices and supporting primary care workers may come to the fore in the future. It would be advisable to use validated clinical risk assessment score systems in clinical practice for decision-making and fast, accurate differential diagnosis.

7. PUBLICATIONS RELATED TO THE THESIS
7.1. ORIGINAL ARTICLES

Pandur Attila, Dr. Eszteri-Regős Renáta, Schiszler Bence, Tóth Balázs, Priskin Gábor, Prof. Dr. Betlehem József, Dr. Radnai Balázs: A klinikai kockázatbecslés jelentősége az akut koronária szindróma betegút csökkentésében. Orv Hetil. 2022; 163(28): 1105–1111. IF: 0,707

Pandur Attila, Schiszler Bence, Tóth Balázs, Priskin Gábor, Sipos Dávid, Prof. Dr. Betlehem József, Dr. Radnai Balázs: Klinikai kockázatbecslésen alapuló döntéshozatal a tüdőemboliás betegek kórházi elbocsátása során. Orv Hetil. 2022; 163(29): 1152–1158. IF: 0,707

Kanyuk, Z., Verzár, Z., Pandur A. (2018). Pulmonális embolizáció. EGÉSZSÉG-AKADÉMIA, 9(1), 25–32.

Pandur A., Banfai, B., Sipos, D., Schiszler, B., Betlehem, J., & Radnai, B. (2018). Risk-stratification and age-adjusted D-dimer test: Are there satisfactory in acute pulmonary embolism? EUROPEAN HEART JOURNAL, 39, 139–139.,

7.2. PRESENTATIONS

Pandur, A ; Schiszler, B ; Tóth, B ; Priskin, G ; Betlehem J, Radnai, B ;

Igazolt pulmonalis embóliás betegek kórházi elbocsátásának lehetőségei – klinikai kockázatbecslés alkalmazása a döntéshozatalban (2022) MESZK Konferencia 2022

Priskin, G ; Pandur, A ; Tóth, B ; Schiszler, B ; Radnai, B ; Betlehem, J

Akut kardiovaszkuláris kórképek a sürgősségi ellátásban grey-zone vizsgálata az NSTEMI betegpopulációban (2022), MESZK Konferencia 2022

Pandur, A., Bánfai, B., Pék, E., Deutsch, K., Radnai, B., & Betlehem, J. (2016b). A pulmonalis embolia diagnosztizálásának költséghatékony megoldásai a sürgősségi ellátásban. In XI. Pécsi Sürgősségi Napok [11th Critical Care Days in Pécs] (pp. 17–17).

Pandur, A., Bánfai-Csonka, H., Bánfai, B., Sipos, D., Schiszler, B., Betlehem, J., & Radnai, B. (2019a). Acute pulmonary embolism in the prehospital emergency care., EMS Madrid 2019

Pandur, A., Bánfai-Csonka, H., Bánfai, B., Sipos, D., Schiszler, B., Betlehem, J., & Radnai, B. (2019c). Risk-stratification and Age-Adjusted D-Dimer test on acute pulmonary embolism.

Pandur, A., Bánfai, B., Sipos, D., Bánfai-Csonka, H., Schiszler, B., Betlehem, J., & Radnai, B. (2019). RISK STRATIFICATION AND AGE-ADJUSTED D-DIMER TEST. In 11. Študentska konferenca s področja zdravstvenih ved z mednarodno udeležbo (pp. 28–28).

Pandur, A., Sipos, D., Banfai, B., Betlehem, J., & Radnai, B. (2019). Age-adjusted D-dimer and risk-stratification in acute pulmonary embolism for reduce the unnecessary CT imaging. INSIGHTS INTO IMAGING, 10(Suppl. 1).

Pandur, A., Bánfai, B., Schiszler, B., Sipos, D., Betlehem, J., & Radnai, B. (2018). DÖNTÉSHOZATAL A SÜRGŐSSÉGI ELLÁTÁSBAN- A PULMONÁLIS EMBOLIZÁCIÓ DIAGNOSZTIZÁLÁSÁNAK LEHETŐSÉGEI. In Tavaszi Szél Konferencia 2018. Nemzetközi Multidiszciplináris Konferencia (pp. 404–404).

Pandur, A., Bánfai, B., Schiszler, B., Sipos, D., Betlehem, J., & Radnai, B. (2017). A pulmonális embólia diagnosztizálásának költséghatékony lehetőségei a sürgősségi ellátásban. In XII. Pécsi Sürgősségi Napok: XII. Critical Care Days in Pécs (pp. 28–28).

Pandur, A., Banfai, B., Radnai, B., & Betlehem, J. (2017). Are the risk stratification methods effective to diagnose pulmonary embolism in patients with heart failure? EUROPEAN JOURNAL OF HEART FAILURE, 19(1. Suppl), 545.

Pandur, A., Bánfai, B., Sipos, D., Schiszler, B., Betlehem, J., & Radnai, B. (2017). Döntéshozatal a sürgősségi ellátásban - A pulmonális embolizáció diagnosztizálásának lehetőségei. In DKK17-Doktoranduszok a Klinikai Kutatásokban absztraktkötet (p. 15).