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ORIGINAL ARTICLE

- 5 Relationship of the Nutritional Status and Handgrip Strength in Military Flying Medical Personnel Gaździńska Agata, Jagielski Paweł, Turczyńska Marta, Bertrandt Jerzy, Gaździński Stefan
- 13 The Incidence of Simulator Sickness in Pilots and Non-Pilots Exposed to Spatial Disorientation Events in the Gyro-Ipt Simulator Lewkowicz Rafał, Bałaj Bibianna, Francuz Piotr
- 26 Development of a Machine-Learning Algorithm for Predicting the Arrival Time and Assessing Factors Influencing Patient Arrival at Hospital Emergency Department – Preliminary Study Karpiel Ilona, Zięba Olga

REVIEW ARTICLE

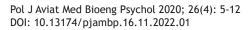
- 37 Effect of Inflammatory Factors in the Pathogenesis of Chronic Rhinosinusitis *Wojdas Andrzej*
- 45 Optical Coherence Tomography and Optical Coherence Tomography Angiography in Ophthalmology Paczwa Katarzyna, Gołębiewska Joanna

REVIEWERS' LIST

55 Reviewers' LIST

INFORMATION

57 Information for Authors





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 - Introduction: The aim of the study was to investigate the relationships between nutritional status and handgrip strength (HGS) of Polish military medical flying personnel.
 - **Methods:** The study was conducted among all active members of the personnel (71 males, 13 females) in Poland. Nutritional status was assessed by anthropometric and body composition measurements.
 - **Results:** Overweight was diagnosed in 47.6% and obesity in 11,9% members. Abdominal obesity was diagnosed in 38.6% of men and 23.1% of women. In women, the mean HGS of the right and the left hand, respectively, was 33.08 ± 3.57 kg and 33.69 ± 2.95 kg. For men, mean HGS of right and left hand were 55.79 ± 7.62 kg and 54.63 ± 7.93 kg, respectively. Furthermore, for men HGS was positively correlated with skeletal muscle mass (r = 0.39), lower limb length (r = 0.33) and chest circumference measured on inspiration (r = 0.33), but not on expiration. There was no significant correlation between HGS, age, and BMI.
 - **Conclusions:** Our study adds to the body of evidence demonstrating an alarmingly high proportion of soldiers with diagnosed obesity. Military medical flight personnel had higher mean handgrip strength as compared to reference values in the male group and in the female group in the left hand. Handgrip strength appears to be related to skeletal muscle mass, similarly to other studies in the general population.
 - Keywords: obesity, overweight, nutritional status, fat mass index, handgrip strength, military flying medical personnel

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IINTRODUCTION

Military flying medical personnel consists of doctors, paramedics and nurses. It is involved in rapid transport of injured (sick) soldiers directly from the battlefield, training ground or military training area to the appropriate medical assistance centres. They are divided into Medical Evacuation Teams (MET). They cooperate with Polish Army units as well as with allied units. Their specialized helicopters and military aircraft are capable of transporting the wounded and injured including those in critical condition. They take part in medical evacuations of civilians as well.

Military service in the air is not typical occupation for medics. This work requires from the military flying medical personnel excellent health condition and appropriate psychological predispositions. The stressful nature of the service may be a factor of many health disorders which, combined with an unhealthy diet, may lead to the development of many metabolic disorders, including obesity.

Proper nutritional status is one of the fundamental factors to maintain high psychophysical performance and good health of military flying medical personnel. Although the nutritional status of the organism is influenced by various factors, i.e., genetic, environmental, sociodemographic and psychological [24], it is fundamental to maintain a proper energy balance, i.e., ensuring a balance between the energy and nutritional value of the food consumed and the amount of energy expenditure associated with daily life activities [14].

Anthropometric examinations and non-invasive bioelectrical impedance analysis (BIA) are commonly used to assess nutritional status [12,25,26]. Another increasingly common anthropometric test is the handgrip strength (HGS) test, which is used to assess muscle strength. According to Massy-Westropp et al. [22], the HGS test is a recommended, inexpensive screening test for assessing muscle strength, non-invasive and easy to perform, with reliability and reproducibility of results, which has been confirmed by validations. In light of reports in recent years this test may be useful in predicting a range of adverse health events. A meta-analysis of 42 studies involving more than three million participants confirmed the relationship between declining handgrip strength with overall mortality, heart disease and cancer [36]. In Poland, the average handgrip strength was 44 kg for males and 30 kg for females (non-dominant hand) [20]. However, differences in the HGS between dominant and non-dominant hand are well described [34].

Hand dynamometer tests have been shown to be a useful tool for assessing strength and functional capacity at work in healthcare workers [23]. According to Leong et al.'s study of 139,691 participants in The Prospective Urban-Rural Epidemiology (PURE) study, increased handgrip strength was associated with young age, male gender, high level of education, employment, high level of physical activity, high calorie intake including high protein intake, with height and weight, and arm circumference [20]. The results of the relationship between age and HGS were heterogeneous in this study and varied between countries and ethnicities.

However, it was demonstrated that grip strength may be affected by fatigue. Wiśniowska et al. [34] demonstrated that in a group of 65 female nurses that the handgrip strength was significantly reduced in both hands after 12-h shift work. Similarly, Tomczak and colleagues demonstrated decreases in maximum handgrip strength due to prolonged exercise combined with sleep deprivation [31,32]. Furthermore, it was demonstrated that higher HGS is associated with higher percentage of percent lean body mass [6]. Similarly, hand grip strength was positively related to muscle mass in female and male young healthy Czech and Slovak students [16].

This study aims to investigate the relationships between nutritional status and grip strength of the upper limbs of Polish military flying medical personnel. We expected a positive relationship of HGS with muscle mass.

MATERIALS AND METHODS

Subjects

The measurements were obtained from all members of active military medical flight personnel in Poland, who reported for obligatory, annual anthropometric examinations to the Laboratory of Dietetics and Obesity Treatment at the Military Institute of Aviation Medicine in Warsaw, Poland, as part of their routine medical examinations. All evaluations were completed between January and December 2019. The study group consisted of 84 persons, including 13 women. The group consisted of 16 physicians, 64 paramedics and 5 nurses. The mean age was 37.75 ± 6.78 years (27 - 55 years). Detailed demographics are presented in Table 1.

Institutional Review Board of the Military Institute of Aviation Medicine, Warsaw, Poland retrospectively agreed to use the results for statistical analyses; therefore, signing informed consent forms was not required (decision no. 9/2021 of August 11th, 2021). All procedures were performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Study design

Nutritional status was assessed by means of anthropometric examinations, with measurements of height and weight, waist, hip and chest circumference measured both on inspiration and expiration. Body mass index (BMI) and body fat distribution index – waist-hip ratio (WHR) were calculated. Waist circumference (WC) alone was also analysed, using the International Diabetes Federation (IDF) criterion [2], which proposes for the European population a cut-off point of 94 cm for men and 80 cm for women.

Body composition was measured using bioelectrical impedance method with the Inbody 370 analyser (InBody, Tokyo, Japan). The degree of overweight and obesity was assessed according to the Body Mass Index (BMI) and body fat content, according to the World Health Organisation (WHO) criteria [9,23].

Body height was measured with a Harpenden Anthropometer (Holtain Ltd, Crosswell, Crymych, Pembs.,UK) to the nearest 1 mm, in standing upright position without shoes. Body weight and body composition were determined after overnight fast.

Handgrip strength (HGS) was measured using a SAEHAN DHD-1 hydraulic medical hand dynamometer (Glanford Electronics Ltd, Scunthorpe, UK). The subjects performed the measurement in standing position with the hand lowered along the body and with the elbow joint straightened.

Three trials each were performed for the right and left hand, with a momentary rest for muscle relaxation. The grip strength was measured in kilograms. The averaged value of the obtained results for each hand was taken for analysis. The values obtained were compared with reference values for the adult Caucasian population [22]. So far in Poland there are no HGS normative values for the adult population aged < 65 years, only for people > 64 years [34].

In our study, all evaluations were performed in morning hours. The participants were asked not to perform any physically demanding tasks at least three days before the examination [31,32]. The participants were asked to empty their bladders before the study. They were in underwear only.

Statistical analysis

The obtained results were subjected to statistical analysis with PS IMAGO PRO 6 (IBM SPSS Statistics 25). Mean values, medians, minima, maxima, and standard deviations were calculated. To check for differences between gender and anthropometric parameters, body composition and HGS, Mann-Whitney U test and chi-square test were used, where appropriate. Spearman correlations were used to test the relationships between handgrip strength and anthropometric parameters separately in men and in women (due to small number of females and due to inter-gender differences in body composition). The level of statistical significance was taken as α <0.05.

Tab. 1. Anthropometric characteristics of the military medical aircraft crew by gender.

Parameter		Total N=84			Males N= 7	1	F	emales N=1	13	-
Parameter	X	SD	Me	х	SD	Me	х	SD	Me	. р
Age [years]	37.75	6.76	36.50	38.03	6.76	37.00	36.23	6.98	34.00	>0.05
Weight [kg]	80.58	12.91	81.80	80.58	12.91	81.80	58.94	5.60	60.10	<0.001
Height [cm]	175.54	8.23	177.00	177.96	6.28	178.50	163.46	5.84	165.00	<0.001
ВМІ	25.93	3.08	25.45	26.63	2.63	26.40	22.12	2.54	22.30	<0.001
Waist [cm]	90.41	9.46	91.00	93.19	7.12	92.00	75.46	5.77	77.00	<0.001
Hip circumference [cm]	99.93	4.97	100.00	100.71	4.34	101.00	87.85	4.24	87.00	<0.001
WHR	0.90	0.07	0.91	0.79	0.05	0.80	0.92	0.05	0.92	<0.001
Chest circumference [cm]	103.37	8.09	105.00	105.62	6.09	106.00	91.08	6.51	90.00	<0.001
Chest circumference on inspiration [cm]	107.43	7.85	108.00	109.72	5.76	110.00	94.92	5.65	95.00	<0.001
Chest circumference on expiration [cm]	101.52	7.90	102.50	103.68	5.97	104.00	89.77	6.82	89.00	<0.001

N - number of participants, X - mean value, SD - standard deviation, Me - median, p - result of the Mann-Whitney U test

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RESULTS

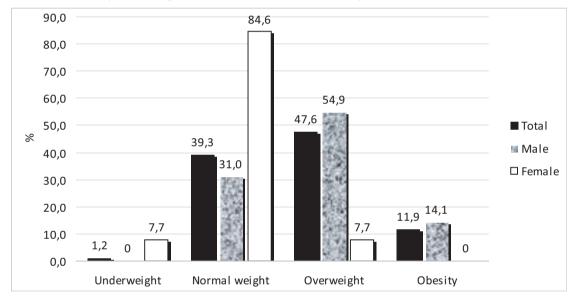
The vast majority of the subjects were nonsmokers (89.3%), with no differences between males and females. Detailed anthropometric characteristics by gender are presented in Table 1. The mean age of respondents was 37.75 ± 6.76 years. Mean BMI of the women was $22.12 \pm 2,54$ kg/m2 and of the men 25.93 ± 3.08 kg/m2.

The normal value of body mass index was found in 39.3% of all medics. Overweight, according to BMI, was diagnosed in 47.6% of the participants, and obesity in 11.9% of all medics studied. Among men, obesity was found in 14%; among women, no obese persons were reported. Detailed results are presented in Figure 1.

Based on waist circumference measurements, abdominal obesity was diagnosed in 38.6% of

men and 23.1% of women. However, when using the diagnostic criteria based on total body fat content [16], obesity was diagnosed only in the male group (see Fig.2.). 46.2% of women were characterised by body fat content below the norm. A detailed summary of body composition parameters by gender is presented in Table 2.

The women's mean right handgrip strength was 33.08 ± 3.57 kg and the left handgrip strength was 33.69 ± 2.95 kg. The left handgrip was higher compared to the reference values for women [20]. The obtained value of the mean right and left handgrip of the male subjects was higher compared to the reference values and was 55.79 ± 7.62 kg and 54.63 ± 7.93 kg for the right and left hand respectively (Table 3). Furthermore, as expected,



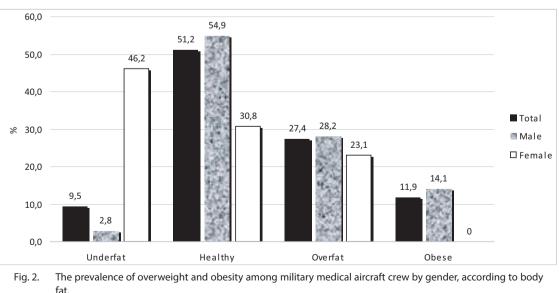


Fig. 1. The prevalence of overweight and obesity in military medical aircraft crew by gender, according to the BMI.

		Total N=84		I	Males N= 7	1	F	emales N=1	13	
Parameter	x	SD	Me	х	SD	Me	х	SD	Me	р
твw [I]	46.85	7.28	48.45	49.32	4.69	48.90	33.36	2.34	32.20	<0.001
Minerals [kg]	4.31	0.70	4.40	4.54	0.50	4.50	3.16	0.26	3.13	<0.001
BFM [kg]	16.46	5.92	14.70	17.06	6.03	16.20	13.45	4.40	13.10	<0.001
SLM [kg]	60.04	9.69	61.50	63.48	6.27	63.00	42.86	3.01	41.30	<0.001
FFM [kg]	64.04	10.02	66.25	67.44	6.45	67.00	45.49	3.23	43.80	<0.001
SMM [kg]	36.17	6.21	37.25	38.39	3.95	38.10	25.07	1.93	24.00	<0.001
PBF [%]	20.31	5.41	20.25	19.92	5.32	19.20	22.44	5.62	21.70	0.119
BMR [kcal]	1743.96	221.30	1776.00	1822.14	144.09	1812.00	1353.08	69.82	1317.00	<0.001

Tab. 2. Body composition parameters of military medical aircraft crew by gender.

N - number of participants, X - mean value, SD - standard deviation, Me - median TBW - Total Body Water, BFM - Body Fat Mass, FFM - Fat Free Mass, SMM - Skeletal Muscle Mass, PBF Percent Body Fat, BMR- Basal Metabolic Rate, WHR - Waist-Hip Ratio, p - result of the Mann-Whitney U test

Tab. 3. Hand Grip Strength in kilograms, for males and females in relation to standards [6].

Hand grip strength	Males	N= 71	Norms 1 30-39		р	Female	s N=13	Norms fo 30-39		р
	x	SD	х	SD		х	SD	х	SD	-
Right hand [kg]	55.79	7.62	47.00	9.70	<0.0001	33.08	3.57	31,00	6,40	0.2502
Left hand [kg]	54.63	7.93	47.00	9.80	<0.0001	33.69	2.95	29,00	6,00	0.0057

N - number of participants, X - mean value, SD - standard deviation, Me - median, p - result of the Mann-Whitney U test

Tab. 4. The results of the correlation of the hand grip strength and other parameters in the group of male.

Parameter	Right	hand	Left hand		
	r	p	r	р	
Length of the lower limb [cm]	0.33	0.005	0.38	0.001	
Chest circumference on inspiration [cm]	0.33	0.004	0.35	0.002	
SMM [kg]	0.39	0.001	0.34	0.004	
BMI	0.08	0.514	0.04	0.765	
Age [years]	0.02	0.836	0.08	0,497	

SMM - Skeletal Muscle Mass, BMI - Body Mass Index, p - result of the Mann-Whitney U test

there was a significant difference between handgrip strength in males and females (p<0.001).

Due to the small number of respondents in the group of women and due to in deniable intergender differences in body composition, the numerical values for correlations between HGS and other variables are presented only for men. Handgrip strength was positively correlated with skeletal muscle mass (r = 0.39, p = 0.001), lower limb length (r = 0.33, p = 0.005) and chest circumference measured on inspiration (r = 0.33, p = 0.004). There was no significant correlation between handgrip strength and age or BMI of the other measured parameters (see Table 4).

DISCUSSION

In this study we evaluated body composition and handgrip strength in all members of military medical flying personnel in Poland. The major finding of this study was a high prevalence of overweight (47.6%) and obesity (11.9%) in this profession. Obesity, according to the WHO definition, was diagnosed only in men. However, abdominal obesity was diagnosed in 38.6% of men and 23.1% of women. Both males and females (left hand) had higher handgrip strength than the reference values for Caucasian population [22], as well as higher compared to the German population, where the average strength of a HGS in women was estimated at 29 kg for the dominant hand and 27 kg for the non-dominant hand; for men 49 kg and 47 kg respectively in the German population [14]. Significantly lower HGS values were also obtained in Brazilian men [8]. The registered grip strength was 47.6 kg for the right hand; 46.3 kg for the left hand; 47.8 kg for the dominant hand; and 46.1 kg in the non-dominant hand. The authors observed a weak and positive relationship between the dominant hand grip strength and height, weight and BMI.

In our research in male participants, HGS was positively correlated with skeletal muscle mass, lower limb length, and chest circumference measured on inspiration. These correlations were not evaluated in females due to the small size of the group.

The elevated prevalence of overweight and obesity is a characteristic feature of many armed forces of developed countries [1,11,13,15,27-29]. Similarly high results of body mass disorders were obtained by Gałązkowski et al. [8] among Helicopter Emergency Medical Service (HEMS) crews in Poland. Based on BMI analysis, it was demonstrated that more than 40% of HEMS crew members were overweight and over 20% were obese, including 3% of the latter suffering from giant obesity (BMI > 40 kg/m2). In our own study, only those with first degree obesity were reported among medics. Even more disturbing results were obtained by Anand et al. among 160 doctors from Delhi, where the prevalence of obesity was over 40% [3]. In comparison with a study of the nutritional status of military medical flying personnel published 10 years earlier by Klos and Bertrandt [18], it should be stated that the nutritional status of the entire medical evacuation system (ME-DAVAC - Medical evacuation) unit crews has improved over the decade. In the cited study, overweight was then reported in 53.3% of physicians and 61.9% of paramedics, and obesity in 20.0% and 16.7%, respectively.

In our study, the majority (85%) of female military medical flight attendants had normal body weight according to the BMI index. Different results were obtained in studies conducted among Polish, Canadian and Scottish nurses, where the percentage of overweight subjects was 44%, 59% and 69%, respectively [17,19,35]. A study by Kyle et al. [19] on the prevalence of obesity among health professionals in England compared with those who work outside the health service found that compared with nurses, the likelihood of obesity was significantly lower for other health professionals (adjusted OR 0.52, 95% CI 0.37-0.75) and higher for non - registered care workers (OR 1.46, 95% CI 1.11-1.93) [28]. The authors found no significant difference in obesity prevalence between nurses and non-health professionals (OR 0.94, 95% CI 0.74-1.18).

Studies on the nutritional status of military flying personnel have shown that maintaining normal body weight is a major problem, especially in the male group. Assessment of nutritional status allows us to determine whether the physiological needs of the examined person are fulfilled in relation to their requirements for nutrients. Studies conducted over the years on the nutritional status of Polish Army soldiers show a frequent occurrence of overweight and obesity in this professional group [4,11,13].

Higher HGS in military flying personnel than in general population may have important metabolic meaning, as an inverse association between muscle strength, chronic disease, all-cause mortality, and cardiovascular-related death has been reported [10,21].

Obesity, mainly abdominal obesity, together with muscle function or the relation fat/muscle is a useful tool for predicting CVD, having a summative effect and greater implication than obesity. Thus, the global management and prevention of CVD should include both the control of excess adiposity and maintenance of adequate/high levels of muscle strength.

In our study, there was no significant correlation between HGS and BMI, as well as between HGS and age. There is a discrepancy in the literature regarding the relationship between HGS and BMI. Many researchers claim that there is a positive correlation between HGS and BMI in both sexes and at all ages [5,7,33]. Stenholm et al., [30] who confirmed the association between obesity and HGS decline in a population of 2,021 Finnish people over 55 years of age, showed that people who maintain a body weight within the normal range during their lifetime are not at risk of as rapid a decline in muscle strength as those with chronic obesity.

Limitations

A limitation of the study was the small number of female subjects, only 13. However, these were all professionally active women among military flying medical personnel in Poland at the time of the study.

CONCLUSIONS

Our study adds to the body of evidence demonstrating an alarmingly high proportion of soldiers with diagnosed obesity. Additionally, military medical flight personnel had higher mean handgrip strength as compared to reference values in the male group and in the female group in the left hand. Finally, handgrip strength appears to be related to skeletal muscle mass, similarly to other studies in the general population. In conclusion, this study described, for the first time, handgrip strength values for the military medical flight personnel in Poland according to nutritional status.

AUTHORS' DECLARATION:

Study Design: Agata Gaździńska, Paweł Jagielski. **Data Collection:** Agata Gaździńska, Marta Turczyńska. **Manuscript preparation:** Agata Gaździńska, Marta Turczyńska, Paweł Jagielski, Stefan Gaździński. The Authors declare that there is no conflict of interest.

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THE INCIDENCE OF SIMULATOR SICKNESS IN PILOTS AND NON-PILOTS EXPOSED TO SPATIAL DISORIENTATION EVENTS IN THE GYRO-IPT SIMULATOR

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- Introduction: A previous study conducted in the Gyro-IPT simulator revealed that applied flight scenarios induced minor severity of simulator sickness symptoms in participants. In this study, however, we did not investigate how the severity of symptoms differs between pilots and non-pilots. Therefore, the presented study aimed to examine whether the symptoms of simulator sickness induced in pilots and non-pilots during spatial disorientation (SD) training are significantly different. We were particularly interested in whether the standard flight scenario used in SD training could be a contributing factor in increasing simulator sickness in novice, inexperienced pilots.
 - Methods: We used the data from the previous study, where 20 male military pilots (age 31.6 ±8.22) with flight experience (total flight hours 1300 ±1167.4) and 20 non-pilots (age 30.9 ±7.72) were assigned to one of two groups and then exposed to a 1-hour long flight session (12 flight profiles, six involved an SD-conflict) with active control in the Gyro IPT simulator. To measure simulator sickness symptoms, the Simulator Sickness Questionnaire (SSQ) was administered pre and post-simulator exposure. In the presented study, the SSQ scores were analyzed independently for the total SSQ and subscores for nausea, oculomotor, and disorientation, and then were compared between groups.
 - **Results:** The score of the total severity and for each subscale of SSQ symptoms in the non-pilots' group were higher than those in the pilots group, however, these differences were not significant. Despite the observed differences, according to the SSQ scoring criteria the simulator sickness symptoms reported by the participants after exposure to the applied flight scenario were negligible.

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Conclusions: The flight scenarios used in SD training did not generate significantly different symptoms of simulator sickness between non-pilots and pilots. The low level of severity of simulator sickness symptoms in these two study groups may indicate difficulty in predicting simulator sickness based on SSQ only.

Keywords: simulator sickness, motion sickness, flight simulator, spatial disorientation, expertise

INTRODUCTION

During and after exposure to different virtual reality environments, such as those created by flight simulators, there is often an adverse phenomenon known as simulator sickness [5,32]. This sickness is referred to when its symptoms result solely from exposure in a simulator and are not present in the real conditions that are reproduced in this device. Simulator sickness can disrupt research measurements [45], negatively influence the effectiveness of training [29], and it may contribute to the interruption of the task performed in the simulator [17,29]. This phenomenon is still an unsolved problem and affects almost every participant in the simulation [20,23,26].

Simulator sickness syndrome

Simulator sickness is a syndrome characterized by a variety of symptoms, many of them motion sickness-like, ranging from malaise, sweating, headaches and dizziness to balance disorders, gastrointestinal disturbances (nausea and vomiting) [36]. Some researchers, however, state that motion sickness tends to be more severe than simulator sickness and that drowsiness does not necessarily indicate simulator sickness [38,74].

Symptoms of simulator sickness and their severity do not only depend on simulator characteristics [21,22,42,43,56,59], but they are also related to scene and scenario design factors [74], user age [40], gender or his/her individual susceptibility to such ailment [6,11] and may increase due to fatigue, alcohol intake [28], as well as anxiety and severe stress [12,32,44].

Simulator sickness in a spatial disorientation simulator

Simulator sickness is a persistent issue in simulator-based training [11,21,32,34], especially in the domain of aviation [10,18,23,46,47,54,55,72,76,77]. It also appears in motion-based simulators as a result of a sensory conflict related to the incongruence of visual and motion cues [34,64].

For many years, a special type of flight simulator has been used in ground-based flight training to demonstrate visual and vestibular in-flight illusions and the loss of spatial orientation phenomenon [51]. This type of simulator, e.g., an Integrated Physiological Trainer (IPT) - the Gyro (Environmental Tectonics Corp., US) uses complex motion and visual stimuli which, under certain conditions, may provoke symptoms of simulator sickness. It has been demonstrated that more than 29% of pilots experience simulator sickness as a result of simulator-based spatial disorientation (SD) training [3]. If simulator sickness occurs, it may reduce the effectiveness of this training, which is an important issue, especially due to the use of SD simulators to teach pilots how to counteract the effects of sensory mismatch during flight. Since the task of the SD simulator is to generate physical stimuli that induce perceptual illusions in pilots, an unpleasant feeling may appear as a side effect of these illusions. Therefore, flight scenarios with motion and visual cues that give the desirable effect (illusion) without any unwanted effects (simulator sickness) should be used in SD simulators.

Due to the fact that some symptoms of simulator sickness may not subside until several hours after leaving the simulator, they may pose a potential threat to flight safety during that time [41,55]. For this reason, a recommendation for a temporary flying restrictions due to exogenous factors affecting aircrew efficiency was made [27]. If, as a result of SD training, a pilot is exhibiting symptoms of simulator sickness, actual flight may not be conducted until 12 hours after such symptoms have completely disappeared.

In the case of the Gyro-IPT simulator, which was applied in our previous studies [2,46,48,50,52,53,75], it was found that restitution of the vestibular system after SD training, performed according to STANAG 3114 [70] and AIR STD 61/117/14 [1], varies individually and usually lasts less than 30 minutes [41]. Based on pilots' vestibular system restitution pattern follow-

ing an exposition in the Gyro-IPT simulator, the researcher [41] evaluated the effects caused by the SD training on the pilots' equilibrium and the impact that it would have on their flight activity and on flight safety. In some pilots, the symptoms of the re-stimulated vestibular system were also observed after the restitution period. However, the researcher [41] did not analyze whether the SD sorties used according to AIR STD 61/117/14 [1] provoke the occurrence of simulator sickness, reducing the effectiveness of training in the Gyro-IPT simulator.

Theories Explaining Simulator/Motion Sickness

There are several theories which have been developed and have even been used to explain why individuals suffer from simulator sickness [74]. These theories relate i.a. to sensory conflicts, postural instability, and the body's response to position. However, none of these theories explain or predict simulator sickness completely. Due to the fact that symptoms of simulator sickness largely overlap with those of motion sickness (motion sickness is a normal physiological response to conflicting sensory stimuli), conflicting cues from the vestibular and visual systems are assumed to have the greatest influence on simulator sickness.

Among the theories that refer to sensory conflicts, the most prevalent in the literature are the 'Sensory Conflict theory' (SC) and 'Subjective Vertical Conflict theory' (SVC). The SC theory was proposed by Reason and Brand [66,67] and then developed by Oman [62,63]. This theory explains motion sickness through a conflict that arises not only between the signals from visual, vestibular and other receptors sensitive to orientation and motion, but also the signals expected by the central nervous system based on previous experience. Therefore, according to this theory, simulator sickness may occur when the received sensory information does not match that which has been retained from immediate past situations.

The SVC theory, used in the second theoretical approach, was described by Bos and Bles [8]. The authors of this theory assumed that all situations that provoke motion sickness are characterized by a state in which the sensed vertical is inconsistent with the subjective vertical, expected based on previous experience [9]. In such a mismatch, a maximum conflict can be assumed in case of a phase difference of 180° between the sensed and expected vertical, and a zero conflict when the detected and expected signals are equal.

Individual differences in susceptibility to simulator sickness and its multisymptomatic nature mean that, despite numerous attempts [14,15,19,24,30,61,73,78], no effective tool has yet been developed to objectively measure the severity of this sickness. Although there are several measures of simulator sickness that can be used in studies where simulator sickness is expected to be a problem, among the most widely used, wellvalidated measure of simulator sickness is the subjective measurement method involving selfassessment with the Simulator Sickness Questionnaire (SSQ) [7,35,38].

Our previous study

In our previous study [48] we examined pilots and non-pilots for their susceptibility to SD when flying in a flight simulator and we verified whether simulator sickness had negligible effect on the results of that study, as it had insignificant effects as a covariate. However, in the presented study we directly compare the severity of simulator sickness symptoms among pilots and non-pilots. On the one hand, according to Miller and Goodson [57] pilots may be more prone to simulator sickness compared to non-pilots due to possible discrepancies between their response to real aircraft characteristics and expected simulator control characteristics. On the other hand, non-pilots who only occasionally, if ever, passively fly do not have a developed habituation to stimuli occurring during actual flight, which may contribute to their increased susceptibility to motion sickness. It is therefore not possible to clearly indicate which of these two groups of people (pilots and nonpilots) will be more susceptible to simulator sickness when exposed to the same flight scenario in a flight simulator. Such knowledge could be useful in developing a simulator training scenario for both pilot candidates and pilots, who due to their little flight experience and/or insufficient vestibular system habituation to the flight environment may have an increased tendency to develop motion sickness during exposition in a flight simulator. Therefore, in the present study, we wanted to evaluate how non-pilots respond, in terms of simulator sickness symptoms, to visual and motion stimuli generated in a simulator during SD training.

The aim of the study

The study aimed to examine whether pilots and non-pilots exposed to the same flight scenario (visual and motion stimuli) in a specially designed flight simulator (spatial disorientation simulator) manifest significantly different severity of simulator sickness symptoms. More precisely, we were interested in whether the standard flight scenarios used in SD training could be a contributing factor in increasing simulator sickness in novice, inexperienced pilots. This study has been performed as part of a larger research in which we analyzed flight performance and instrument scanning strategy during SD events [2]. Thus, the results presented in this paper are derived from a reanalysis of the data we collected in that earlier study.

The inclusion of the non-pilots' group in this study allowed us to examine how simulator-generated SD cues affect, in term of simulator sickness, people who do not actively fly (do not expect stimuli that occur in a real flight) or fly passively (as a passenger) only occasionally (have a minor habituation to stimuli occurring in real flight). On the other hand, pilots are a group of people who expect simulator control characteristics to be the same as that of a real aircraft. Moreover, some of them are unfamiliar with the stimuli that induce in-flight visual and vestibular illusions and have no experience of exposure to simulator-induced SD events; the latter was an inclusion criterion in our study. For this reason, we expect that they will also be, to some extent, susceptible to the motion sickness caused by illusions related to sensory conflict generated in the simulator.

METHOD

Study design

To compare the severity of simulator sickness symptoms among pilots and non-pilots, the between-group study design consisted of an experiment in which participants performed flying tasks in an SD simulator was used. The experiment consisted of carrying out maneuvers with the maintenance of flight parameters according to the flying instructions given in defined standard flight scenarios. To rule out the influence of exposition in a flight simulator on simulator sickness incidence, the participants completed the Polish version of the Simulator Sickness Questionnaire (SSQ) [7].

Participants

The forty volunteers (20 pilots aged 31.6 \pm 8.22, and with a flight experience of 1300 \pm 1167.4 total flight hours; 20 non-pilots aged 30.95 \pm 7.72) were recruited to perform a flight simulator experiment, conducted according to the SD training program in the Military Institute of Aviation Medicine (WIML) (Warsaw, Poland). The inclusion criteria

were healthy, active flying male pilot (fixed-wing aircraft) or non-pilot between the age of 20 to 55, with normal or corrected to normal vision and no history of neurological disorders, especially any negative clinical history of vestibular symptoms e.g., dizziness, vertigo, or disorientation. Moreover, none of the voluntaries reported any history of severe motion sickness or simulator sickness.

All participants were male, Polish military aviators actively flying fixed-wing military aircraft (M-28M, CASA C-295M, MiG-29, F-16, and M-346 Master) with no experience of exposure to simulatorinduced SD. All non-pilots had no previous flying experience. All participants reported normal sleep patterns and avoided alcohol 24 hours prior to the study.

The protocol study was approved by the Ethical Committee (Institute of Psychology at the John Paul II Catholic University of Lublin, Poland) and an informed consent form was completed by each participant prior to the experiment. All subjects were paid for their participation.

Stimuli and apparatus

Flight simulator. To demonstrate the SD event the spatial disorientation Gyro-IPT (Integrated Physiological Trainer) simulator (Environmental Tectonics Corporation, Inc., Southampton, US), located at the Military Institute of Aviation Medicine (WIML, Poland) was used. This dynamic motionbased simulator with 3-degrees of freedom (roll $\pm 30^{\circ}$, pitch $\pm 15^{\circ}$, and yaw 360°) has a one-channel, non-collimated out-the-window visual display (with a total field-of-view ~40° horizontally by ~28° vertically). Although the simulator does not represent the aircraft that the pilots normally fly (the motions are generated by the simulation model of the TS-11 Polish jet trainer aircraft), the flight instruments displayed in the cabin represent typical indicators that are applied in the pilots' aircraft.

The Gyro-IPT is particularly recommended for the training of pilots in evoked SD condition [16]. This training follows NATO Standardisation Agreement (STANAG) Number 3114 (Aeromedical Training of Flight Personnel) [70] with general recommendations concerning ground-based demonstration and training (AIR STD 61/117/14) [1].

Stimuli. The set visual, vestibular and auditory cues were included in defined twelve flight scenarios. The flight profiles comprised of general maneuvers in a fixed-wing aircraft. The following six well-known visual and vestibular-origin illusions [16,65] were implemented in the six flight profiles:

- daytime false horizon illusion (caused by a sloping cloud deck) included in the straight and level flight (S&LF) profile;
- constant shape illusion (caused by an up-sloping runway) implemented in a circle-to-land procedure (C-T-LP) at nighttime;
- constant size illusion (caused by a narrowerthan-usual runway) included in a straight-in approach (S-IA) profile at nighttime;
- somatogyral illusion (caused by erroneous perception of the strength and direction of actual rotation the false sensation or lack of rotational motion) induced in a straight and level flight after a left turn (S&LFALT) at daytime, during flight in clouds;
- Coriolis illusion (created by cross-coupled stimulation of semicircular canals when there is a change of head position during rotational motion) induced in a right banked turn (RBT) at daytime;
- leans illusion (caused by the limited sensitivity of vestibular organs) induced in a straight and level flight after a right turn (S&LFART) at nighttime.

Each flight profile was presented in two conditions, the disorientation condition (conflict flight), in which visual or vestibular disorientation cues were present, and the control condition (nonconflict flight), in which these specific disorientation cues were absent. The remaining parts of the flight profiles were kept the same for the control and disorientation conditions. All the participants flew the same profiles (a total of 12 flight profiles) List of basic flight profile parameters is given in Table 1, whereas detailed description of the applied flight profiles, including the specifications of stimuli and flight instrument manipulation is presented in our earlier papers [49].

Simulator Sickness Questionnaire. Although the results of some studies [19,31,58,60,73,79], which are based on the measurement of specific physiological parameters seem promising for evaluating simulator sickness, they are still an auxiliary method for questionnaires such as SSQ. Therefore, to examine whether motion sickness during flights in the SD trainer had occurred, a Polish version of the Simulator Sickness Questionnaire (SSQ) [7] was administered.

The SSQ is widely used in studies on the SD to rule out the influence of simulator sickness on flight and cognitive performance. This questionnaire consists of 16 symptoms regarding motion sickness that can be caused in a flight simulator, which are rated in terms of severity (0 – none, 1 – slight, 2 – moderate, 3 – severe) and then are summed to yield three subscale scores (a nausea score, an oculomotor score, a disorientation score), and a total score.

Procedure

The course of study in a flight simulator included familiarizing and training flight (for pilots and non-pilots, respectively) and the main exposition consisted of 12 flight profiles (six conflict flights and six non-conflict flights). Participants were randomly assigned to compose a study group. They

Flight profile	Duration of profile [s]	Disorientation condition	Control condition	Flight instrument manipulation
The Circle-To-Land Procedure (C-T-LP)	166 ^a	Nighttime runway up-sloped 10°	No up-sloped runway	None
Straight-and-Level Flight (S&LF)	190	Slope of cloud deck tilted 10° rightward from 19,000 ft to 21,000 ft	No tilt of the cloud deck	From 130 s to 160 s blackout of attitude director indicator
Straight-In Approach (S-IA)	90 ^a	Nighttime runway narrowed in width from 300 ft to 150 ft	Runway 300 ft wide	None
Straight-and-Level Flight After Left Turn (S&LFALT)	290	76°·S ⁻¹ of sustained yaw (at 0.4°·S ⁻²) stop yaw rotation in 217 s of flight (at -15°·S ⁻²)	No programmed acceleration stimulus	None
Right Banked Turn (RBT)	210	70°·s ⁻¹ of sustained yaw (at 0.5°·s ⁻²) stop yaw rotation in 173 s of flight (at -2°·s ⁻²)	No programmed acceleration stimulus	None
Straight-and-Level Flight After Right Turn (S&LFART)	150	68°·s ⁻¹ of sustained yaw (at 1°·s ⁻²) stop yaw rotation in 84 s of flight (at -4°·s ⁻²)	No programmed acceleration stimulus	From 92 s to 105 s blackout of attitude director indicator

Tab. 1. List of parameters of the flight profiles.

Note. ^a or runway level achieved

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Nausea SSQ-N	Oculomotor SSQ-O	Disorientation SSQ-D
General discomfort	General discomfort	Difficulty focusing
Increased salivation	Fatigue	Nausea
Sweating	Headache	Fullness of head
Nausea	Eye strain	Blurred vision
Fullness of head	Difficulty focusing	Dizzy (eyes closed)
Stomach awareness	Difficulty concentrating	Dizzy (eyes opened)
Burping	Blurred vision	Vertigo

were only briefed with all relevant flight related requirements, but were not introduced to the flight scenario and purpose of research.

The participants were in full control of simulator flying. The non-pilots were trained in the procedures for maintaining straight-and-level flight, turning with 30 deg bank angle, changing attitude and approach-to-landing maneuver. This training was to ensure that all non-pilots could demonstrate a basic level of eye-hand coordination proficiency in flying the simulator. The minimum proficiency required is detailed in the paper [49]. The training flight lasted for approximately 30 minutes. Only participants who achieved the required level of proficiency could participate in the study (the main exposition consisted of 12 flight profiles).

To get acquainted with operational characteristics of the simulator all pilots were given 5-10 minutes of "free-flight." This familiarization flight profile included the basic elements of pilotage with the approach-to-landing maneuver. If a pilot reached a given target attitude, heading, vertical speed, bank (within the same acceptable deviations as for non-pilots), he could participate in the study.

The participants (pilots and non-pilots) performed maneuvers with the maintenance of flight parameters according to the flying instructions given (recorded commands). The order of flight profiles (six conflict flights and six non-conflict flights) was fixed at random. Participants did not know the order of profiles and which of them were conflict flights.

To rule out the influence of exposition in the simulator on simulator sickness incidence and ensure that participants did not feel sick before the main part of experiment (12 flight profiles), they completed the form concerning their health condition (i.a. physical fitness, previous motion sickness episodes, taking medicines or alcohol during the last 24 hrs). Immediately following the main exposition in the simulator (12 flight profiles), the SSQ [7] was administered to obtain simulator sick-

ness ratings. After completing the questionnaire, all participants were debriefed and paid. Finally, prior to the participant leaving the study, the researcher ensured that any simulator-induced sickness symptoms had subsided.

The duration of a single experiment did not exceed 60 minutes (not including training or familiarization flight). All participants completed the study at the same time of day (between 10:00 and 16:00).

Measurements

SSQ data were rated regarding severity and then were summed to yield three subscale scores: nausea score (SSQ-N), oculomotor disturbances score (SSQ-O), disorientation score (SSQ-D), and total severity score (SSQ-TS). The SSQ symptoms included in each subscale score are given in Table 2.

Mean SSQ scores that were obtained after completing all flight profiles were determined based on pre-defined factor weightings suggested by Kennedy et al. [38]. These factors are obtained by adding up the results of all relevant items (each factor consists of 7 items) and multiplying this sum by the specified weight; for nausea factor by 9.54 (scores ranging from 0 to 200.34), for oculomotor factor by 7.58 (with scores ranging from 0 to 159.18), and for disorientation factor by 13.92 (scores ranging from 0 to 292.32) [21]. Finally, the scoring criteria of SSQ that reflect the severity of simulator sickness symptoms was applied [71].

Statistical Analysis

To compare the effect of the between factors that are represented by the group type (pilots' and non-pilots' groups) a t-student test was used. The t-test was run on the recorded mean scores of SSQ, and was performed for each subscale of SSQ symptoms (nausea SSQ-N, oculomotor SSQ-O, and disorientation SSQ-D) separately. A significance level of p = 0.05 was considered statistically significant and was set for all analyses. For all statistical analysis IBM SPSS version 17.0 (IBM Corporation, US) was used.

	Tab. 3.	The t-test results and the mear	n scores of SSQ symptoms	for each subscales and e	xperimental conditions.
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Subscale of SSQ	Group	o type		Statistic	al results	
symptoms	Pilots	Non-Pilots	t	df	р	Cohen's d
Nausea SSQ-N	1.46 (2.51)	1.79 (1.88)	-0.478	36	0.635	0.12
Oculomotor SSQ-O	3.41 (2.12)	4.33 (2.76)	-0.969	36	0.339	0.32
Disorientation SSQ-D	1.90 (1.63)	2.31 (1.21)	-0.609	37	0.546	0.22
Total SSQ-TS	2.25 (1.52)	2.81 (1.95)	-1.537	37	0.133	0.27

Note. values represent mean and standard deviation

RESULTS

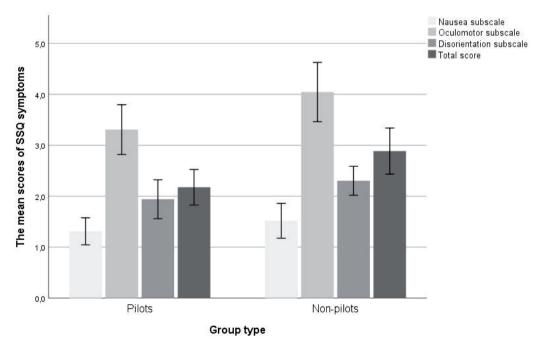
Overall, in our study, the occurrence of simulator sickness symptoms (measured by SSQ) was reported by approx. 30 % of participants. All of the reported symptoms remained in a low severity and no discomfort was reported both in pilots and non-pilots [71]. There were no differences between pilots and non-pilots in total scores of SSQ (SSQ-TS t(37) = -1.537, p = 0.133). The commonly reported symptoms were general discomfort, difficulty focusing, dizziness with eyes opened, and fullness of head. The mean scores of SSQ symptoms for each analyzed subscales of SSQ symptoms and study groups are shown in Table 3.

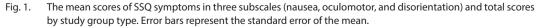
The t-test performed separately for each subscale of SSQ symptoms (SSQ-N, SSQ-O, and SSQ-D), and for the total score of SSQ symptoms showed no significant differences between the symptoms reported by the study groups (pilots and non-pilots). The results of the t-test are shown in Table 3.

The mean scores of SSQ symptoms for each subscales and study groups are given in Fig. 1.

DISCUSSION

Our study revealed that according to the SSQ scoring criteria [71], the symptoms of simulator sickness reported by pilots and non-pilots after exposure to the standard flight scenario were negligible. It also implies that the Gyro-IPT simulator did not produce symptoms of simulator sickness which would raise concern for post-simulator exposure activities.





Differences in severity of simulator sickness symptoms

The incidence of simulator sickness between the pilots' and non-pilots' group does not significantly differ at total severity score (SSQ-TS) and for each subscale of SSQ symptoms (Tab. 3, Fig. 1). The non-pilots' group reported a higher severity of simulator sickness symptoms (MSSQ-TS=2.81) compared to the group of pilots (MSSQ-TS=2.25) performing the same task, under the same conditions. Although, this outcome - symptoms of simulator sickness - is negligible [71], the higher severity of the symptoms in the non-pilots' group is not surprising. The non-pilots' group consisted of people who do not fly or only occasionally fly passively. Pilots, on the other hand, actively fly, which may result in habituation of their vestibular system to motion stimuli generated in the Gyro-IPT simulator [4]. Such habituation may decrease the simulator sickness symptoms' severity. Additionally, it is worth noting that the lack of statistical significant difference between the group of pilots and non-pilots may also indicate that pilots who participate in SD training after extended break in flying or minor flight activity will not be at risk of simulator sickness.

The eye movement disturbances, which refer to the oculomotor subscale, are more common symptoms in the non-pilots' group (MSSQ-O=4.33) than in the pilots' group (MSSQ-O=3.41). This result can be explained by the fact that the non-pilots' group does not hold the appropriate aviation authority-issued medical certificate, which all pilots hold. It mainly concerns the test of the vestibular system, which is important in the regulation of the vestibular-ocular reflex. Vestibular system impairments may manifest themselves in nystagmus, which can be induced by a kinetic stimulus (e.g. motion generated by the simulator cabin). The difficulty with focusing eyesight increased from 20% to 67%, and the general discomfort of pilots increased from 27% to 45% [77]. It is also confirmed by our results of oculomotor activity (MSSQ-O=3.41) which have the highest value among the other analyzed subscales of SSQ symptoms.

Another explanation for the lack of differences between the group of pilots and non-pilots may be explained by the fact that stimuli (visual and motion) applied in the flight scenarios might not be strong enough to show differences in susceptibility to simulator sickness between these study groups.

Finally, it should be noted that due to the small effect size (Cohen's d, Tab. 3) and sample size, the

above-discussed results of the study may not be representative. This observation is also confirmed by the low statistical power (not exceeding 0.25) which means that there is a high probability of an erroneous conclusion that there is no effect (no statistically significant difference between the groups) when one may actually exist. To increase the power of the study, a larger sample size and/ or interventions to increase the effect size would need to be considered.

Reasons for the low severity of simulator sickness symptoms

Due to the severity of simulator sickness symptoms being positively correlated with the duration of simulator exposure [33,39], slightly stronger symptoms of this sickness could be expected in our study. Such relation of simulator sickness and the time spent in a simulator is explained by researchers [64] by the visuo-vestibular mismatch. In our study, the participants were given a single simulator exposure for a period not exceeding 60 minutes, while Cobb et al. [17] indicated that simulator sickness symptoms' severity steadily increases for up to one hour during simulator exposure exceeding 30 minutes. Similarly, Wojciechowski and Błaszczyk [77] point out that when training lasted longer than 60 minutes, as many as 85% of respondents felt more tired, while in sessions lasting less than 1 hour only 33% of the respondents complained about such ailment. In our study, therefore, the duration of simulator exposure (up to 60 minutes) might have not been the reason for occurrence of severe symptoms of simulator sickness. On the other hand, the results of a recent study [68], indicate that the duration of exposure in a more advanced SD simulator (AirFox Disorientation Simulator; AMST-Systemtechnik GmbH, Austria) lasting 45 minutes might have been the reason for occurrence of simulator sickness.

Field of view (FOV) is another factor which may have influenced the severity of simulator sickness symptoms in our study. Several studies [37,42] have revealed that using a wide FOV in a simulator display system makes individuals more prone to simulator sickness. It has been found [55,64], that a FOV of >60° induces a large optical flow and is conducive to simulator sickness. In the present study, the Gyro-IPT simulator has a narrow FOV (a total field of view of ~40° horizontally by ~28° vertically) that may explain the low score of simulator sickness symptoms.

Moreover, in some flight scenarios, to induce some SD illusions a degraded visual environment, e.g., by clouds in the flight profile with somatogyral illusion (S&LFALT), or by nighttime in the flight profile with leans illusion (S&LFART), was administrated. Thus, by weakening the impact of visual cues on the pilot's ability to maintain spatial orientation, in line with the sensory conflict theory of motion sickness, we expected the occurrence of more severe symptoms of motion sickness than those observed. Probably the lack of visual cues, displayed outside the virtual cockpit may not have been enought to trigger a more severe sensory (visual-vestibular) conflict.

When analysing other factors influencing simulator sickness, several relevant individual factors should be mentioned, such as age, gender, health status and flight experience. Some of them e.g., sex, were considered in the criteria for exclusion from our study. Kolasinski [42] and Johnson [33] found that medication and alcohol intake also predispose simulator users to become simulator sick. In our study, the participants were healthy and avoided alcohol 24 hours prior to the study thereby reducing the risk of simulator sickness.

The studies [40,69] on simulator sickness in younger and older adults revealed that the latter experienced significantly more simulator sickness than younger adults. Moreover, prolonged experiences of sickness were observed to a greater extent in older adults than younger adults. Renjhen (2018) also found that the older experienced pilots have more severe symptoms of simulator sickness than the younger pilots. The group of pilots and non-pilots in our study consisted of both older (above 39 years old) and younger adults participants (less than 26 yerrs old), therefore, the differences in simulator sickness scores due to the participant's age are not assessable.

Another reason for the low severity of motion sickness symptoms in our study may be that the applied flight scenery was simple [74]. When the scene presented during the simulation is too complex, this may cause an increase in the severity of symptoms [37]. Moreover, there were also no freeze or reset commands and no flying backwards scenarios in our study, which according to Johnson [33] are conducive to simulator sickness.

Finally, a pilot is also particularly susceptible to simulator sickness when there are discrepancies between his/her expected simulator control characteristics and the response to real aircraft characteristics [57]. It is worth mentioning that the SD simulator used in our study does not replicate characteristics of the aircraft that the pilots normally fly (in this simulator the stimuli are generated by the simulation model of the TS-11 Polish jet trainer aircraft). Wherefore, the pilots, who were actively controlling the flight simulator, may have been more prone to simulator sickness than non-pilots, who due to the lack of flight experience, could not demonstrate specific sensory expectations.

Study limitation and further considerations

In this study, the participants were exposed to both motion and visual stimuli simultaneously during one flight sortie. While motion stimuli predominate in vestibular illusions (flight profiles at night or in clouds without visibility of the natural horizon, where stimuli are limited to the indications of flight instruments), visual stimuli are mainly involved in profiles with visual illusion (false horizon illusion, size illusion, and shape illusion). Therefore, we were unable to evaluate which of these stimuli (visual or motion) had a greater impact on the reported incidence and severity of simulator sickness.

Moreover, the study involved non-pilots who had not been previously tested for vestibular dysfunction and susceptibility to motion sickness. They also do not hold the appropriate aviation authority-issued medical certificate, which confirms i.a. the health condition of the pilot's vestibular system. Although they had not any history of prior episodes of motion or simulator sickness prior to the study (inclusion criteria), we cannot be completely assured that individuals in this group were not susceptible to motion sickness. Johnson [33] indicated that people who have such a history of sickness are more likely to experience simulator sickness. For screening non-pilots' susceptibility to motion sickness and to ensure that they did not differ from groups of pilots with respect to their susceptibility to motion sickness, the Motion Sickness Susceptibility Questionnaire [25] should be used.

Furthermore, to replicate an in-flight illusion, the flight profile applied in this study requires much higher angular velocities and accelerations in the SD simulator than those that occur in the actual flight scenario. Despite this, the symptoms of simulator sickness appeared to be negligible and the differences between these symptoms reported by the pilots and non-pilots were statistically insignificant. It might be anticipated that with a stronger stimulus and/or a longer exposure time, the effect of higher angular velocities and accelerations would have become evident.

We also observed that the participant perceives the symptoms of the simulation sickness if they are strong enough. The development of the simulator sickness symptoms is initially not noticeable by the participant, which means that the effect of a motion sickness triggering stimulus on participant performance starts before the participant realizes that he/she is affected by this sickness. By using objective methods of measuring simulator sickness, e.g. by measuring psychophysiological responses, it would be possible to observe the changes that usually occur before the participant is aware of any of them.

The last major limitation of our study is the small sample size, which was beyond our control. This was due to the fact that the data reanalysed in the presented study were collected previously in another research [2]. This problem would not exist if the effect size was larger (Tab. 3). It would then be possible to draw conclusions about detected differences between groups with greater certainty.

CONCLUSION

The present study considered whether pilots and non-pilots exposed to the same stimuli during piloting the Gyro-IPT simulator manifest different severity of simulator sickness symptoms. The non-pilots group consisted of people who, due to lack of flight experience, could not expect, during exposure in the simulator, the stimuli that occur in a real flight and have not had the opportunity to become habituated to such stimuli. We conducted this study because we were interested in whether the standard flight scenarios used in SD training could be a contributing factor in increasing simulator sickness in novice, inexperienced pilots.

We found that among 30% of participants who reported symptoms of simulator sickness, the severity of these symptoms was negligible. It can therefore be concluded that simulator sickness did not have a negative impact on the SD demonstration during the training performed according to STANAG 3114 [70] and AIR STD 61/117/14 [1].

By investigating the role of flying experience in simulator sickness episodes we found, that simulator sickness symptoms reported by pilots and non-pilots after SD training, were not significantly different. Nevertheless, our findings (although not statistically significant and with low statistical power) suggest that pilots are less prone to motion sickness than non-pilots.

On the other hand, such a low level of severity of simulator sickness symptoms in these two study groups (pilots and non-pilots) may indicate the difficulty in predicting simulator sickness based on the SSQ only. Therefore, the use of objective indicators based on the measurement of physiological parameters should be considered in the assessment of the severity of simulator sickness, as studied by other researchers [58,74,79].

Finally, although our study results did not show influences of the standard flight scenarios used in SD training on the occurrence of simulator sickness, it is worth recalling a few preventive measures, which should be used when possible to help reduce this sickness. These measures may include monitoring and screening participants, controlling environmental conditions, and adjusting the scenarios and protocol. Based on the findings of previous studies [13,36,39] and their summaries [74,77], we would like to remind the readers of a few more important principles for reducing the incidnce of simulator sickness:

- individuals who have not previously had contact with the simulator or who had a long break from the last simulator exposure are at risk of simulator sickness,
- training / exposure in the simulator should not exceed 1 hour in one session, breaks should be planned,
- the simulator session should be the shorter the more intense it is,
- the simulator cabin should be kept cool and well-ventilated,
- participants should be screened to exclude those who are particularly susceptible to simulator sickness, such as those who have recently taken drugs or alcohol, or report fatigue, lack of sleep, cold or infection (e.g., ear or an upper respiratory infection).

AUTHORS' DECLARATION:

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DEVELOPMENT OF A MACHINE-LEARNING ALGORITHM FOR PREDICTING THE ARRIVAL TIME AND ASSESSING FACTORS INFLUENCING PATIENT ARRIVAL AT HOSPITAL EMERGENCY DEPARTMENT – PRELIMINARY STUDY

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Abstract: Healthcare is one of the most important topics affecting society. Emergency Departments (ED) play an important role in the patient treatment cycle, providing immediate and primary health care as well as access to services offered by hospitals. From a hospital's perspective, it is crucial that emergency departments are well organized in each hospital sector. One of the most important yet overlooked problems in the medical industry is emergency department congestion.

An attempt was made to estimate and predict, using predictive models and machine learning algorithm techniques, the impact of factors on the arrival time of patients at hospital emergency department and to verify the effectiveness of teaching the models, along with a comparison which one is the best in predicting the phenomena. Research materials were source data from the 2018 National Hospital Ambulatory Medical Care Survey (NHAMCS) – Emergency Department.

In this paper, a study was conducted to search for factors that could affect the frequent arrival of patients at emergency departments. A tool for predicting the expected arrival time, taking into account the current arduous conditions/factors in the ED, has the potential to improve situational awareness and contribute to mitigating problems related to congestion. It appears that the model can be used to enhance decision support systems by determining patient arrival times.

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The results obtained in the random forest regression algorithm are estimated at R2 of 86% and RMSE of 5.45. For research purposes, when attempting to analyze on a sample and reliable hospital department database, the random forest regressor method identified the most relevant factors such as initial vital signs.

The results obtained allow for a broader view in the context of assessing the prevailing situation in the emergency department. In this case – examining the most relevant factors influencing patient arrival times. With the results of high effectiveness, an algorithm can be designed to assist emergency departments in proper monitoring of existing problems.

Keywords: machine learning, databases, hospital system, data analysis, Emergency Departments

INTRODUCTION

Healthcare is one of the most important topics affecting society. Emergency departments play an important role in the patient treatment cycle, providing immediate and primary health care as well as access to services offered by hospitals [4,47]. Taking care of patients in an appropriate and timely manner, as well as making the right decisions regarding patient admission, is a major challenge for healthcare services [4]. From a hospital's perspective, it is crucial that emergency departments are well organized in each hospital sector. Given its key position in the organizational structure of the hospital, a poorly functioning Hospital Emergency Department (HED) affects accurate decisionmaking in the hospital unit [3]. One of the most important yet overlooked problems in the medical industry is emergency department congestion [16,18,29]. Emergency departments in European countries and the US are seeing record numbers of patients presenting [47]. These are the most severely injured individuals or those requiring immediate care. It is often very difficult to immediately determine the condition of all patients present in the emergency department when rapid intervention is required. Actions taken under the pressure of increasing life-threatening risks and the number of patients waiting for help result in wrong decisions and sometimes delays that quickly lead to hospital overcrowding [37]. When this occurs, hospitals are unable to admit patients on time, or the waiting time for treatment increases significantly [5]. The problem of hospital overcrowding may seem easy, but is is actually very difficult to solve [37]. Patients who have been admitted but have to wait a long time in the emergency department, often with high anxiety levels, can lose trust in healthcare systems. If emergency departments function poorly, this threatens not only the health and safety of the patient, but also the public's trust in the health service [3]. Another important aspect raised in the effective functioning of the emergency department and efficient recording of patient flow is the triage. A proper triage system that categorizes patients into correct priorities is equally key to increasing safety and better management of emergency patients. The current triage system in Poland is not sufficiently effective [35,47]. It is therefore necessary to develop an innovative approach to solve this global problem so as to improve patient flow and prevent the reorganization of hospital operations [37]. The health service must provide care to a large number of patients, many of whom are in critical condition. Healthcare professionals should be able to guickly access patient information and clinical data for immediate decision-making [47]. However, a person's ability to multitask is very limited and making a diagnosis is often difficult. An effective and robust methodology would allow early detection of diseases and could be used by physicians as a decision aid. Therefore, disciplines such as statistics and computer science are essential in supporting medical research. These disciplines are faced with the challenge of discovering new techniques beyond the traditional ones [4]. An essential tool supporting physicians and ED staff is artificial intelligence [47], especially machine learning (ML) [9,13,21,22,40,43,44], which utilizes various algorithms. The past five years have seen an increase in the number of applications of Artificial Intelligence (AI) and machine learning in various sectors of the economy, including healthcare, which has yielded many impressive advances, from autonomous driving to drug discovery. With the development of AI, algorithms, and machine learning technologies that are essential in searching for solutions to problems in the medical sector, various opportunities have emerged to guide future development

efforts. Just a few years ago, despite enthusiasm among researchers, acceptance of new technologies in the medical space was both enthusiastic and cautious. The introduction of new technologies into a complex system in the medical sector often yields unpredictable results. Despite this uncertainty, it is optimistic to look at new technologies through the lens of existing treatment paradigms to predict how patient outcomes can be affected and potentially improved. The current generation of machine learning systems in medicine is largely aimed at limited diagnostic aids in radiology, cardiology and pathology. Examples of Al-based systems include Computer Tomography (CT) brain hemorrhage detection, systems for detecting lung nodules and coronary calcification, as well as echocardiography tools. Existing advanced systems tend to focus on problems for which a solution is readily achievable within the timeframe of the treatment cycle. This has led to the development of systems with varying degrees of clinical utility in emergency departments. It can be said that the direction of the thriving implementation of artificial intelligence in emergency departments is the same as in other medical and non-medical fields. The initiation of AI deployments will provide access to systems that are clinically relevant but narrowly applicable. As systems mature, some routine patient care tasks will be automated and decision-making in cognitive tasks will be aided by AI systems [31].

The research problem is an attempt to predict and estimate, using the development of predictive models and machine learning algorithm techniques, the impact of factors on the time of patients arrival at the hospital emergency department, and to verify the effectiveness of teaching the models, along with a comparison which one is the best in predicting the phenomena.

MATERIALS AND METHODS

Source data from the 2018 National Hospital Ambulatory Medical Care Survey (NHAMCS) -Emergency Department, which was made publicly available on the CDC government website (www.cdc.gov) as an IBM SPSS data file, was used as research material. The NHAMCS survey is based on outpatient visits to physicians and hospital emergency rooms over a 12-month period and is designed to collect data on the use of outpatient care services. It covers all fifty U.S. states and the District of Columbia and is a nationwide sample of non-institutional general and short-stay hospitals, excluding federal, military and veterans hospitals. The original database contains a total of 20,291 records and 946 columns. The overall data analysis, including data preparation and the development of predictive models, was performed using the Jupyter and RStudio environments, which use Python and R languages with libraries for analysis and design of machine learning algorithms. The study applied machine learning and used algorithms for supervised learning to solve the set objective. Regression algorithms were used to develop predictive models. The data collected were sorted and assigned to the appropriate groups, as shown in Figure 1.

Data Preparation

The downloaded SPSS .sav database source file was first converted to a Microsoft Excel spreadsheet file. The database, an excerpt of which is shown in Figure 2, comprises 948 columns, which

А	AI	AJ	AK	AL
Variable	IMMEDR	PAINSCALE	SEEN72	RFV1
Question	Immediacy with which patient should be seen (unimputed)	Pain scale (0-10)	Was patient seen in this ED within the last 72 hours?	Patient's complaint, symptom, or other reason for v
Subquestion				
Scale	Unknown	Unknown	Unknown	Unknown
Missings				
Values/Labels	-9 Blank	-9 Blank	-9 Blank	-9 Blank
	-8 Unknown	-8 Unknown	-8 Unknown	10050 Chills
	0 No triage for this visit but ESA does conduct triage		-7 Not applicable	10100 Fever
	1 Immediate		1 Yes	10120 Other symptoms of body temperature
	2 Emergent		2 No	10121 Feeling cold
	3 Urgent			10122 Feeling hot
	4 Semi-urgent			10123 Feeling hot and cold
	5 Nonurgent			10150 Tiredness, exhaustion
	7 Visit occurred in ESA that does not conduct nursing triage			10200 General weakness
				10250 General ill feeling
				10300 Fainting (syncope)
				10350 Symptoms of fluid abnormalities
				10351 Edema
				10352 Excessive sweating, perspiration
				10353 Excessive thirst
				10400 Weight gain
				10450 Weight loss
				10451 Recent weight loss
				10452 Underweight
				10460 Symptoms of face, not elsewhere class
				10500 Chest pain and related symptoms
				10501 Chest pain
				10502 Chest discomfort, pressure, tightness
				10503 Burning sensation in the chest
				10550 Pain, specified site not referable to

Fig. 1. Excerpt of coding in the data file (own elaboration). Screenshot from own research.

<class 'pandas.core.frame.DataFrame'> RangeIndex: 19351 entries, 0 to 19350 Columns: 203 entries, arrival_time_nums to patient_code dtypes: float64(64), int64(139) memory usage: 30.0 MB

	arrival_time_nums	month_of_visit	day_of_week_of_visit	wait_time_to_first_provider	length_of_visit_in_minutes	patient_age_in_years	age_recode	age_
0	20	12	1	21.0	93.0	5	1	
1	19	12	1	12.0	48.0	5	1	
2	14	12	6	21.0	99.0	0	1	
3	17	12	4	59.0	493.0	21	2	
4	17	11	2	25.0	117.0	26	3	

5 rows × 203 columns

Fig. 2. Database (own elaboration). Screenshot from own research.

were then truncated to 203 columns and 19,351 rows since the removed portion represented empty records. Features that are redundant and will not be relevant to the analysis were omitted. The spreadsheet thus reworked serves as the basis for working on the data for further analysis. The data preparation and analysis process for further predictive analysis involved loading the necessary libraries for specific functions required in further analysis, including analytical libraries, feature selection functions, individual types of predictive models, and predictive statistics of the models. In addition, the subsequent steps checked whether the database had actually been coded correctly. The database contained negative values, which according to the coding meant empty. Negative values were converted to empty for the sake of preserving the principle of feature transformation, and then the data cleaning process was carried out. This stage of data mining is very important because in the further modeling process, machine learning algorithms underperform or completely fail if the input data, through its variability, introduces unwanted distortions and noise. The arrival time target variable, which was encoded in military time format, was then verified. Such a format is impractical for analysis, so an hourly record was extracted. This format is more suitable for analysis, yielding more reliable and standardized results. The correctly prepared file formed the basis on which the target analysis was carried out.

Selection of Relevant Features

After the exploratory process, we proceeded to generate a function that would return the most important features in the clustering method in order to determine which of them has the greatest impact on multidimensional scaling. Correlations of the independent variables were then verified. Two methods were chosen to select the most relevant variables and the best data sample. The first method is correlation, i.e. calculating the significance of the effect between the variables x and y. The correlation results show that the data varies too much, which means that common features cannot be easily identified in the analyzed database. The second method, namely PCA, is a feature clustering technique. It is one of the so-called sensitivity analyses and involves demonstrating significance based on variance. The database was clustered into 12 divisions. Next, the cluster that provided the best results in terms of the variance of relationships in the clustering of these variables was calculated. The variance of the variables is referred to as variance. The most significant variables with the highest variance were selected for further analysis. Figure 3 below shows a set of the most relevant variables from the entire range of features in the database, which will be used in further data modeling analysis.

Variable	PCA_Value	
medication_1	62185.230416	0
patient's_complaint_symptom_or_other_reason_fo	45055.997491	1
patient's_complaint_symptom_or_other_reason_fo	42913.881816	2
index	1340.348556	3
length_of_visit_in_minutes	20.471795	4
length_of_stay_in_observation_unit_in_minutes	19.619153	5
hospital_number	15.843903	6
initial_vital_sign_heart_rate_per_minute	8.339000	7
wait_time_to_first_provider	6.262934	8
initial vital sign temperature	4.668952	9

Fig. 3. The most relevant values (own elaboration). Screenshot from own research.

Breakdown of the Data Set

Initially, the explanatory variables, or model predictors x and y, were defined. Then, in order to be able to teach and test the effectiveness of generating predictors, the dataset was randomly divided into a training dataset and a test dataset, in which 30% of the data was taken to test the model. The training set consisted of the remainder of

```
y = databank.czas_przybycia_nums
X = df_pca
X_train, X_test, y_train, y_test = train_test_split(X, y, test_size=0.3)
Fig.4. An excerpt from the code of the algorithm used to break down the set. Screenshot from own research.
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the data used to build the model. The following is an excerpt from the code (Figure 4) for the breakdown of the set used in the predictive model.

Training and Model Selection

Regression models are among the most widely used, practiced and developed methods in the context of analyzing large data sets. The main idea of regression is the process of predicting and forecasting data for a particular variable in relation to other variables. In other words, it is the process of fitting a variable to a newly created one according to a previously learned pattern. Prediction is possible once a regression model has been built on the basis of analysis, which will predict the value of a given characteristic based on an assumed statistical error [36]. A description of the regression models that were used in the analysis is presented below:

Linear regression – a basic type of regression in statistical analysis. It assumes a linear relationship between the explained variable and the explanatory variable, similar to correlation. It is assumed that an increase in one variable causes an increase or decrease in the other. The regression function in this case is linear [34].

Ridge regression – another approach to estimate the coefficients of models with highly correlated independent variables. It was developed to address the issue of imprecise least squares estimators in linear regression models where the independent variables are highly correlated with other independent variables. Therefore, as a solution, a ridge regression estimator was created to provide a more accurate estimation of the ridge parameters. Variance and mean squared estimators are often smaller than the previously obtained least squares estimators [46].

Decision tree – builds regression or classification models in the form of a tree structure. It breaks the dataset into smaller and smaller subsets, while incrementally expanding the associated decision tree. The end result is a tree with decision nodes and leaf nodes. A decision node has two or more branches, each representing values for the attribute under study. A leaf node represents a decision for a numerical target. The highest decision node in the tree, which corresponds to the best predictor, is called the root node. Decision trees can handle both categorical and numerical data [48].

Random forest regression - each decision tree has a high variance. However, if each of these trees is combined together in parallel, then the resulting variance is low because each decision tree is perfectly trained on that particular sample of data and therefore the result does not depend on one decision tree, but on many. For a classification problem, the final result is obtained by using a classifier with majority voting. In the case of a regression problem, the final result is the average of all results. Random forest is an ensemble technique capable of performing both regression and classification tasks using multiple decision trees and a technique called bootstrap and aggregation, commonly known as bagging or containerization. The basic idea behind this technique is to combine multiple decision trees to determine the final outcome, instead of relying on individual decision trees. A random forest has multiple decision trees as underlying learning models. Random sampling of rows and features from the dataset is performed, creating sample datasets for each model [49].

Gradient enhancement – enhancement algorithms are among the most common and widely used algorithms. They are considered one of the most powerful predictive modeling techniques. The basic principle of boosting, like other clustering algorithms, is to combine several weak "students" into a single, stronger one. It involves using basic machine learning models, sequentially one after the other, that fail to adequately predict outcomes. Each subsequent model attempts to correct the errors of its predecessor. Eventually, the models are combined to build one strong model [23].

RESEARCH SCENARIOS

In order to extend the analysis regarding the prediction of visits or emergency arrivals to hospital emergency departments, calendar variables such as time of day, day of the week, month or holidays and other special events, as well as mass events, can be used as predictors. In addition, variables from the environment, such as weather conditions or seasons, can be used. It can be speculated that weather conditions such as high winds, thunderstorms, tornadoes, floods and the day after rainfall may affect the ED arrival rate. An increase in the number of patients in emergency departments can also be seen on a certain day of the week or a certain time of the year. Using weekday trends and weather forecasts, emergency departments would be able to anticipate the number of patients and adjust their staff and resources accordingly. In article [6], patterns of emergency care use during different seasons was analyzed and the percentage of days with each weather factor and the percentage of visits were compared. The data indicated that the season has a strong influence on the use of medical care services in EDs, as it affects the incidence of illness and injury. In contrast, extremely cold and stormy conditions significantly reduced emergency department use, but an estimated 80–95% of expected visits occur on days with poor weather conditions [10].

RESULTS AND DISCUSSION

In this study, the predictions were based on ML models whose performance is equivalent or better than that of other studies. A study was conducted to search for factors that could influence the frequent arrival of patients to emergency departments. A tool for predicting the expected arrival time, taking into account the current arduous conditions/factors in the ED, has the potential to improve situational awareness and contribute to mitigating problems related to congestion. The model can be used to enhance decision support systems by determining patient arrival time.

The presented approach can be used as a tool to support the process of medical staff scheduling in order to effectively manage a hospital department. The proposed model can be used as an objective tool for the hospital to allocate and activate resources, e.g. preparing additional beds, calling in nurses.

Results of Quantitative and Qualitative Analysis

Based on the summary results of the predictive accuracy indicators presented in Table 1, it is possible to infer which model is best suited for determining predictions for the analyzed data

Tab. 1. Performance indicators of models. Own research.

set and whether it is possible to estimate by how much the model will be wrong in the next observation. The dependent variable is the arrival time, in hours. In contrast, the root means squared error of the forecast (RMSE) is given in the same unit as the target.

The above results of the model accuracy assessment (Tab.1) show that the best model for predicting phenomena is the random forest regression model. This is mainly indicated by the coefficient of determination R2, the optimal score for which, according to the literature review, is estimated to be between 0 and 1, while the higher the score, the more accurate the model is and the smaller the difference between the estimated and actual value. The random forest regression model score was estimated to be 86% and the RMSE statistical error was 5.45. The results of the RMSE coefficient were selected using the GridSearchCV function, which, through a grid search method, compares all combinations of parameters and returns those with the best fit to the model. Optimizing models by tuning them with hyperparameters is one of the most important steps in machine learning. It improves model performance by finding optimal values for hyperparameters. The GridSearchCV function used is a technique for finding the best parameter values from a given set of parameter grids [2,32]. Basically, it is a k-fold cross-validation method where the given dataset is split into k consecutive folds. The set is still divided into training and testing. Each iteration keeps one partition for testing and the remaining k-1 partitions for training the model. This is repeated until each iteration has been used for testing. At each iteration, the function records the performance of the model, and finally provides an average of all the performances. This is also a time-consuming process. It is a technique for improving and enhancing model performance. The lower the score obtained, the better the model is. Figure 5 presents the result of the algorithm. The random forest regression model predicted the most relevant factors affecting the predicted target variable, such as initial vital signs-temperature and time to first medical contact.

Method	R2	RMSE [h]
Linear regression	0.01517	5.53
Ridge regression	0.01328	5.49
Decision tree regression	1.0	5.49
Random forest regression	0.85838	5.45
Gradient boosting Regression	0.15707	5.45

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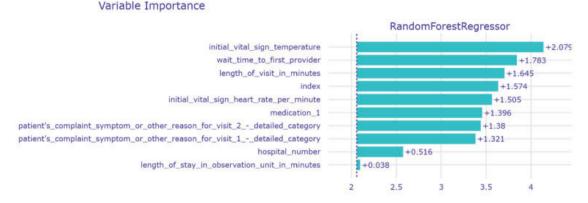


Fig. 5. A selection of the most significant factors affecting the arrival time of patients to the emergency department (own elaboration). Screenshot from own research.

Applications

The purpose of this study was to predict and estimate the impact of different factors on the arrival time at HEM through the use of predictive models and machine learning algorithm techniques. The work also had a subordinate purpose of analyzing medical data using machine learning algorithms to optimize the future management process in hospital emergency departments. The reference point for the analysis is the presentation of theoretical issues regarding the current organization of an ED, which are the cause of the malfunctioning of this department and the growth of management problems, i.e. the increase in patient congestion in the hospital departments and the lack of an organized patient flow, as well as the mishandling of operations from an organizational perspective. With an understanding of the current disorganization of the departments, possible solutions to this problem are also described, citing those already in use [5,8]. Tools used in the field of Artificial Intelligence and Machine Learning are an indispensable support in the search for solutions to problems in the medical sector. Therefore, in this paper, a study was conducted, using a reliable database, to look for factors that can influence the frequent arrival of patients to emergency departments. A tool for predicting relevant factors affecting the arrival time would have the potential to improve situational awareness and contribute to counteracting crowding problems. In order to search for the best model, a comparative analysis of five Machine Learning (ML) algorithms (linear regression, ridge regression, decision tree regression, random forest regression, gradient enhancement) that differ in their training mechanism was conducted. As a result of the analyses, the random forest regression model was found to be the best-fitting model for predicting significant factors affecting

patient arrival time with the best coefficient of determination score of 86% and the lowest RMSE error rate of 5.45. It was noted that only one model was the best in terms of predictive performance, training time and interpretability. The random forest method identified the most significant variables such as initial vital signs-temperature and then time to first medical contact. These variables appear to be of little importance to the problem posed when determining the impact of individual factors on arrival times, while they performed well in training the model, as confirmed by the results of the predictive statistics obtained. The other models did not prove their effectiveness. Due to an overly diverse database in terms of divergence and randomness of individual patient values, and the lack of additional variables such as weather conditions, which could highlight new patterns unattainable by the tested model, it is hard to pinpoint the time series in which one might expect a higher intensity of ED visits. In summary, the results indicate that ML algorithms can accurately predict the impact of factors on patient arrival times to HEDs. The analysis of the selection of relevant features by applying ML algorithms for patient arrival time not only fulfilled one of the research objectives but was also used in further analysis - Machine Learning. The results estimated by the algorithms indicate a correctly selected predictive modeling technique, which worked well with the variables contained in the database. The solution used in the paper was presented as an example of the use of ML techniques aimed at using the solution in emergency departments. The ML approach presented herein can serve as a tool to assist in building medical staff schedules and can be integrated, for example, into a human resources system to effectively manage and miti-

gate the utilization of hospital emergency department resources. ML models can also be applied to, for example, symptom-targeted data, enabling earlier interventions using advanced diagnostics and tailoring better and cost-effective personalized therapies. The proposed model can be used as an objective tool for the hospital to allocate and activate resources, e.g. calling in nurses and doctors, preparing additional beds for patients, and consulting with admitting physicians about alternative treatments in other hospital units. In practice, the forecasting model can be put into everyday clinical use by augmenting existing decision support systems that track patients in the ED or by adding an estimate of the number of patients expected to arrive within a certain time frame.

Measures to improve the efficient management of HEDs play an important role in improving the quality of health care. Of particular importance is the knowledge of what solutions can be introduced, and what solutions applied in other countries, for example, have proved successful. The phenomenon of overcrowding in emergency departments, which is common both in Poland and worldwide, has led to a desire to solve this problem. The research work sought a pattern through the use of Machine Learning techniques.

Arrival time to the HED

Arrival time is of great importance to healthcare [8,42,50,51]. Patient flow through emergency departments (ED), overcrowding and long waiting times are acknowledged as increasing worldwide issues in healthcare [11,52]. Overcrowding in emergency departments is a serious problem in many countries. Accurate ED patient arrival forecasts can serve as a management baseline to better allocate ED personnel and medical resources. Zhang et al. [45] presented two methods of features for forecasting patient arrivals. Their results showed that for hourly forecasting of patient arrivals, each machine learning model performs better than the traditional Auto Regressive Integrated Moving Average (ARIMA) model. Accurate information about arrival times, the number of patients that can reach the hospital, can be used as a basis for management to better allocate staff, adapt rooms or free up beds [1,12,20]. Patient arrivals are determined by many variables and are extremely unpredictable. However, research shows that machine learning algorithms can significantly improve time prediction performance [19,25,28,38] and a number of proposed solutions is growing [7,14,24,26,41].

The arrival time issue is also analyzed in relation to patients with acute ischemic stroke. There is a great need to find a way to reduce the time to get to the hospital and to predict when patients will arrive [17]. The arrival time or the mentioned weather conditions, for example, are considered to be deeply related to the issue of patient forecasting for proactive bed management [20]. In 2022, Huang et al. [15] presented analyzes of clinical and sociodemographic factors in relation to arrival time on Kinmen Island. This study investigated factors associated with delayed emergency treatment of patients with Acute Myocardial Infarction (AMI) on Kinmen Island and offered suggestions for developing interventions to reduce the time from symptom onset to receipt of appropriate medical care [27,30].

The causes of overcrowding are important for many reasons and have implications for patient arrival times or patient handling times by medical staff [33,39,42]. It is worth noting that changes in meteorological factors beyond a certain range can cause thermal imbalances in the body, which can promote the development of many diseases [53], also affecting both the arrival time and the number of patients in hospitals.

CONCLUSION

The research objective was achieved through the use of an accurate random forest regression algorithm, as confirmed by the obtained metrics of R2 accuracy of 86% and RMSE of 5.45. For research purposes, when attempting to analyze on a sample and reliable hospital ward database, the random forest regressor method identified the most relevant factors such as initial vital signs - temperature and then the time of waiting for the first contact with a physician. To improve forward-looking analysis for predicting visits or emergency arrivals to hospital emergency departments, calendar data such as hour, day of the week or month, can be used as predictors. Also, other special events or atmospheric variables, such as weather conditions or season, can be taken into account.

The presented approach can be used as a tool supporting the process of building a work schedule for medical staff in order to effectively manage a hospital ward. The proposed model can be used as an objective tool for the hospital to allocate and activate resources, e.g. opening additional beds, and calling nurses. Our research is basic, giving some insight into the situations that it is advisable to continue.

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Conceptualization: Olga Zięba. Methodology: Olga Zięba. **Validation:** Ilona Karpiel, Olga Zięba. **Resources:** Ilona Karpiel. **Data curation:** Olga Zięba. **Writing-original draft preparation:** Ilona Karpiel, Olga Zięba. **Writing-review and editing:** Ilona Karpiel, Olga Zięba. **Supervision:** Olga Zięba, Ilona Karpiel. **Project administration:** Olga Zięba. **Funding acquisition:** Olga Zięba. The Authors declare that there is no conflict of interest.

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Original Article

- 47. Materiały badawcze opracowane w ramach prac B+R w projekcie DOBBI010/19/02/2020 Opracowanie nowoczesnego modelu zarządzania pacjentem w stanie zagrożenia życia w oparciu o samouczącą się algorytmizację procesów decyzyjnych i analizę danych z procesów terapeutycznych. 2020.
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EFFECT OF INFLAMMATORY FACTORS IN THE PATHOGENESIS OF CHRONIC RHINOSINUSITIS

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Abstract: Both immune mechanisms, involved in inflammatory processes induced by viral and bacterial pathogens or allergy-inducing agents, and non-immune mechanisms play a direct role in the pathogenesis of chronic rhinosinusitis (CRS).

Contrary to popular belief, bacterial infection plays a much smaller role. As a rule, this is a secondary process – following the development of inflammatory processes in the mucosa of the paranasal sinuses, its defense mechanisms are disrupted, which promotes the development of infection. Bacterial infection of the paranasal sinuses is associated with the formation of a biofilm responsible for the persistence of rhinosinusitis, or bacterial endotoxins acting as superantigens cause the persistence of the inflammatory process.

The main role in the inflammatory process is played by CD4+ and CD8+T lymphocytes, as the centers regulating cytotoxic and humoral immune responses. They act in various ways, mainly cytotoxic, and as such can interact with virtually all nucleated host cells showing expression of antigens of endogenous origin and through cytokines, mainly pro-inflammatory cytokines, and they increase migration of inflammatory cells into the mucosa of the nasal cavity and paranasal sinuses. The paper discusses in detail the interaction of immunocompetent cells and their impact on chronic inflammatory processes in the mucosa of paranasal sinuses.

Atopy is another factor contributing to the CRS, increasing the action of pro-inflammatory cytokines and promoting processes that lead to obstruction of the ostiomeatal complex.

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The complexity of the clinical picture of the CRS in relation to ongoing research on pathogenesis indicates that it is still not possible to strictly define the phenotypes of the disease.

Keywords: chronic rhinosinusitis, pathogenesis, CD4+ T lymphocytes, CD8+ T lymphocyte, cytokines, biofilm, atopy

INTRODUCTION

The nasal cavity and paranasal sinuses are an area of constant contact with the external environment and are subject to a number of infectious agents and a variety of protein structures. In its development, the human body has developed physical and immunological defense mechanisms to maintain the integrity of the respiratory system. These include the airway epithelium, mucociliary transport, as well as cellular and humoral immune mechanisms. If the defense mechanisms are broken, a germ enters the body and the inflammatory process develops. The resulting rhinosinusitis may disappear quickly and completely, or it may progress to a chronic inflammatory process [16].

CLASSIFICATION OF CHRONIC RHUNOSINUSITIS

According to current classifications, chronic rhinosinusitis (CRS) is a common clinical picture of a heterogeneous group of diseases with complex pathogenesis. In addition, the clinical picture of chronic rhinosinusitis consists of symptoms from other organs caused by various factors. Rhinosinusitis significantly affects the quality of life of patients. The rich symptomatology of the disease negatively affects their daily functioning [9,36].

The authors of the latest EPOS 2020 proposed another change in the division of the chronic rhinosinusitis. Currently, we divide chronic inflammation into primary CRS and secondary CRS. In addition, depending on the anatomical extent of the inflammatory lesions, into a localized or generalized form [16].

RISK FACTORS FOR CHRONIC SINUSINITIS

CRS is the subject of ongoing research and clinical observations to gain more knowledge on the pathogenesis of the disease. At least several hypotheses have been formulated in recent years that point to possible etiopathogenetic factors, including: conditioning by fungal infection, bacterial biofilm formation, the presence of a superantigen, the influence of eicosanoids, the importance of the microbiome and the immune barrier [28,49].

At the core of the consideration of the phenotypes of the CRS are the anatomical and functional conditions of the upper respiratory tract, i.e., the ostiomeatal complex, which are de facto responsible for shaping the clinical picture of the disease.

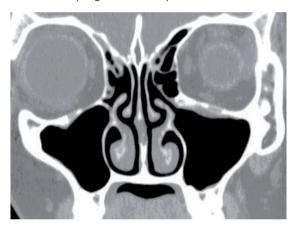


Fig. 1. Distribution of tympanograms of the right ear in group I in subsequent examinations.

The ostiomeatal complex (Fig. 1) is a functional structure in the anterior ethmoidal complex, which is the final common drainage and ventilation pathway of the frontal sinus, maxillary sinus and anterior ethmoidal cells. This space, which is limited medially by the middle nasal concha, laterally by the orbital plate, and on the top and in the back by the basal lamina of the middle nasal concha, includes: the middle nasal meatus, the ethmoidal infundibulum, the frontal recess, and the orifice of the maxillary sinus and anterior ethmoidal cells. The mucus drainage pathway from the aforementioned paranasal sinuses passes through here. For this reason, the region of the ostiomeatal complex is responsible for proper drainage and ventilation of the paranasal sinuses. Any disruption of mucociliary transport in this region can lead to the development of inflammatory changes in the maxillary sinuses, frontal sinuses and anterior ethmoidal cells [27,46].

The primary role in the defense mechanism of the paranasal sinuses is played by the mucociliary apparatus [47]. A properly functioning mucociliary transport mechanism allows the nasal and paranasal sinus mucosa to be constantly covered with a fresh, moist layer of mucus that renews itself every quarter of an hour. Ciliary cells and mucus play a primary role in mucociliary transport. The mucus transport is carried out toward the head, toward the nasal part of the throat. The movement of secretions in the paranasal sinuses toward natural outlets follows well-defined pathways [12,22].

Determination of the CRS by fungal infection formed the basis of the first hypothesis of pathogenesis, which was formulated by researchers at the Mayo Clinic in the US. This is because they detected the presence of airborne fungal elements in the patients' nasal and sinus structures. It was later shown in in vitro studies that Altenaria antigens can induce peripheral mononuclear hyperreactivity and enhance eosinophil migration and degranulation [8,13,23,37,48].

It is now accepted that the presence of fungi and their colonization may play an important role in modifying the clinical picture of the disease. This is because they contain proteolytic enzymes that can induce the release of inflammatory cytokines and a response involving Th2 lymphocytes. They may be responsible for the formation of a distinct phenotype of the CRS [35,39].

Another of the factors mentioned is bacterial biofilm. Bacterial biofilm formation is associated with the presence of bacterial infection, which is found in the nasal cavity and paranasal sinuses in 42-75% of those undergoing surgical treatment [11,18,42]. Colonization by microorganisms is possible due to their adhesive properties, and the structure of the resulting biofilm is stabilized by EPS (extracellular polymeric substances), forming the so-called glycocalyx. The mature form of the biofilm is surrounded by a thick layer of glycocalyx, to which minerals, organic compounds and cells of other microorganisms are adsorbed. The EPS includes polysaccharides, the largest fraction, as well as some proteins, nucleic acids, surfactants, lipids and water [18,25,36].

Biofilm formation is a multi-step process. A bacterial biofilm is a three-dimensional structure made up of microcolonies and glycocalyx. Microcolonies are separated by a network of open tubules, through which nutrients are transported and metabolic products removed. It is estimated that bacteria make up only 15% of the biofilm. Despite this structure, bacteria living inside the biofilm are exposed to oxygen limitation and therefore their metabolism changes – the activity of anaerobic metabolic pathways (desulfurification, denitrfication and fermentation) is increased, and the synthesis of certain enzymes (e.g. proteases, phospholipase C) and toxins is inhibited [10,18].

The adaptation of bacteria living in the biofilm to survive in harsh conditions also forces phenotypic changes, and there may be induction of point mutations of genes whose expression products increase the level of resistance of individual cells in the biofilm. Within the biofilm, horizontal gene transfer occurs. Plasmid transmission is one of the important mechanisms for the spread of resistance to drugs, disinfectants or other chemical agents. Horizontal gene exchange increases microorganisms' chances of survival.

According to the literature, bacterial biofilm is present in 70-75% of patients with the CRS. Gender, classification, duration of the disease, as well as the use of intranasal steroids and antibiotics were found to have no significant effect on its presence in the sinuses, subject to a chronic inflammatory process. Studies of patients undergoing functional endoscopic sinus surgery confirm the recurrence of biofilm, as it was found to be present again after surgical treatment in up to more than 70% of patients [15,17,21,42,44,51].

BACTERIOLOGY IN CHRONIC RHINOSINUSINITIS

Sinus infections occur in 80% of cases directly through the mucous membrane of the nasal cavity, and less frequently through the bloodstream or dental route. Rhinoviruses, coronaviruses, influenza viruses and parainfluenza viruses cause most colds, which are followed by a complication of acute rhinosinusitis in 10-15% of cases. Bacteria are present in 60% of cases of acute rhinosinusitis (ARS). The most common bacterial pathogens isolated from the material collected from sinuses are: Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis. Rarer pathogens are anaerobic bacteria and Staphylococcus aureus.

Based on the literature, the primary pathogens of the CRS in adults are Streptococcus pneumoniae (20-40%), Haemophilus influenze (30-40%) and Moraxella catarrhalis (30-40%). Others also include Staphylococcus aureus. In the Doyle et al. study, Staphylococcus aureus accounted for 32% of paranasal sinus infections, while in the Tan et al. this percentage exceeded 56% of the patient group studied. The number of strains cultured usually depends on the size of the patient group studied. It is increasingly believed that staphylococcus aureus colonization occurs with increased frequency in patients with chronic rhinosinusitis with polyps, but not in patients without nasal polyps. The literature reports 21 classical pathogens and 61 non-classical pathogens in chronic rhinosinusitis. In some cases, rhinosinusitis is referred to as idiopathic [20,24,36,42,50].

Several mechanisms of bacterial action in this disease are assumed: it may be secondary to an existing inflammatory process. The presence of bacteria is the cause of the development of inflammation, bacterial biofilm is responsible for the persistence of rhinosinusitis or bacterial endotoxins acting as superantigens cause the persistence of the inflammatory process.

The demonstration that the presence of a superantigen produced by staphylococci enhances the local eosinophilic response was the basis for another hypothesis for the pathogenesis of the CRS [3].

Superantigens are proteins with high molecular weight and produced by various microorganisms (bacteria, fungi and viruses). Unlike classical antigens, superantigens bind directly to the major histocompatibility complex MHC class II outside the antigen binding site, which positively promotes the stimulation of large numbers of T lymphocytes. They stimulate several clones of lymphocytes, specifically recognizing the antigen, comparable to classical antigens, but all lymphocytes, having a given type of Vb chain, belonging to different clones, regardless of the specificity of the TCR. Thus, superantigens cause activation and polyclonal proliferation of CD4+ and CD8+ lymphocytes in the tissue and peripheral blood, in the case of certain superantigens this refers to up to 5-30% of all lymphocytes. The number of stimulated lymphocytes is thus 10-100 times greater than in the case of a reaction with a classical antigen [4,40].

The detection of immunoglobulin E directed against Staphylococcus aureus enterotoxins A and B (Staphylococcus aureus SEA and SEB) in nasal polyp homogenate confirmed for the first time that superantigens may play a role in the pathogenesis of nasal polyps and eosinophilic inflammation of the nasal cavity and paranasal sinuses. Tissue eosinophilia appears to be of primary importance in the development of the CRS, where its severity shows a positive correlation with the severity of the clinical course of the disease and the development of polyps when the level of eosinophils is high. Secreting a variety of inflammatory mediators, eosinophils, neutrophils, lymphocytes, macrophages and mast cells also affect the progression of changes observed in the inflammatory process [26].

Currently, it is accepted that staphylococcal superantigens can modify the clinical picture and course of the disease, promote the development of polyps, but it is difficult to consider them as an etiologic factor of the CRS [1,2,26,52].

ALLERGY AND CHRONIC RHINOSINUSINITIS

A broader look at allergic mechanisms points to the possible role of allergic mechanisms in shaping the clinical picture of the disease. It is known that allergic rhinitis can cause and can aggravate the course of sinusitis. Swelling of the nasal mucosa, regardless of the cause, impedes ventilation and drainage of the paranasal sinuses, which, of course, definitely increases the risk of their inflammation. Therefore, the thesis that atopy predisposes to inflammation of the nasal mucosa of paranasal sinuses seems an obvious assumption. Abnormalities in the ostiomeatal complex contribute to sinus disease, and allergic rhinitis, characterized by mucosal swelling, can lead to reduced sinus ventilation and mucus retention, creating favorable conditions for the development of infection. Epidemiological data indicate that such a link is probable. In addition, evidence of common pathophysiological mechanisms links these diseases. Although a causal relationship has not been definitively clarified, there is a growing number of research supporting the credibility of reports that atopy is co-responsible in the development of the CRS [19,27].

Bousquet et al. [7], Hellings et al. [19], Lin et al. [32] report that 40% of patients with the CRS are also found to have allergic rhinitis. The association of the two diseases in many other studies ranged from 25% to 70%, depending on the criteria used and the study method. In recent years, a number of studies have attempted to prove that allergic mechanisms play an important role in the development of the CRS in patients suffering from an allergy – these mechanisms activate locally in the paranasal sinus mucosa. In their study, Shaw et al. [38] obtained a significant increase in mast cells in the sinus mucosa in patients suffering from CRS with polyps, regardless of the coexistence of atopy [6,7,19,33,34,38,41].

The effect of eicosanoid (eicosanoid hypothesis) on the occurrence of the CRS has been addressed in terms of aspirin intolerance and nasal polyp formation. The abnormal pathway of eicosanoid metabolism revealed in this process, along with increased production of pro-inflammatory leukotrienes and decreased synthesis of anti-inflammatory prostaglandins, indicated their role in shaping the pathology in the course of the disease [47].

Leukotrienes, which play a key role in allergic rhinitis, have been found to be present in chronic sinusitis, especially if there is an increased count of eosinophils. Tan et al. [43] in their study evaluated the prevalence of positive skin tests in patients with the CRS. They obtained results that differed significantly from other epidemiological studies. Positive results of the test were obtained for 82% of patients with chronic rhinosinusitis, most of which involved allergy to dust mites and ragweed pollen. In contrast, Leo et al. [30] found that the prevalence of allergy to airborne allergens in children with CRS was comparable to the general population of children in Italian society, and recommended not including routine allergy testing in the diagnosis of CRS. Lill et al. [31] did not confirm the high correlation of food allergy and CRS with nasal polyps. In their study, they found that 14% of patients with CRS were diagnosed with cow's milk allergy and 15% of patients were diagnosed with dust and cereal pollen allergy [30,31,41,43].

An interesting study was conducted by Liu [33], evaluating a possible link between the CRS resulting from food allergy and strong immunomodulation of Staphylococcal enterotoxin B from Staphylococcus aureus. The presence of enterotoxin B increases the dominant role of the Th2 lymphocyte, while at the same time causing an increased response of the sinus mucosa in the coexistence of food allergy. Serum levels of lymphocytes and a range of interleukins (IL-4; IL-13; IFN-y) were assessed and nasal lavage fluid culture test was performed. The results of in vitro studies also showed a role for enterotoxin B in the increased response of Th2 lymphocytes to food allergens, compared to a group of patients with CRS but without food allergy [33,34].

CRS is characterized by changes in the mucous membrane of the sinuses. These include goblet cell hyperplasia, limited subepithelial edema, cellular infiltration and foci of fibrosis [16,51].

DISCUSSION

In the course of the CRS, there is an increase in the number of inflammatory cells such as mast cells, lymphocytes, macrophages, dendritic cells, eosinophils, basophils and neutrophils infiltrating the mucosa. In allergic CRS, increased IL-4 synthesis, increased transformation into Th2 lymphocytes, and increased IL-13 levels are observed in the mucosa after exposure to the allergen. The consequence of this process is an increased release of humoral pro-inflammatory factors, such as cytokines and growth factors [45,46].

The importance of the microbiome (microbiome hypothesis) in the pathogenesis of the CRS has been suggested based on the observation that externally induced changes in the gastrointestinal microbiome, leading to the development of secondary intestinal flora, can affect chronic inflammation. The microorganisms that make up the microbiome have the ability to produce antibacterial proteins and lipids that enable them to maintain homeostasis by depressing pathogen growth. This phenomenon is interpreted as a restoration of the microbiome via probiotics or inoculation of "healthy" bacteria that will help to cure the inflammation [5,14,29,46-48,51].

So far, studies and clinical observations have only pointed out the possibility that changes in the microbiome may be involved in the course of chronic inflammatory diseases, but so far there is no convincing evidence of a role in the pathogenesis of the CRS.

The importance of the immune barrier (immune barrier hypothesis) in chronic inflammation has long been known. Disruption of the physical barrier associated with the anatomy of the nasal cavity and paranasal sinuses, as well as damage to the natural immune response, can lead to the development of the lesions seen in the CRS [12].

On the basis of currently available research results, it can be concluded that immune mechanisms, especially the disruption of the natural response, significantly affect the course of chronic inflammation, but they cannot be singled out as the sole factor responsible for causing the CS [23].

CONCLUSIONS

In conclusion, the complexity of the clinical picture of the chronic rhinosinusitis in relation to ongoing research on pathogenesis indicates that it is still not possible to strictly define the phenotypes of the disease. The involvement of immune mechanisms in the observed inflammatory process, regardless of the etiological factor, is undeniable. On the other hand, the influence of environmental factors can shape the clinical picture of the disease.

AUTHORS' DECLARATION:

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OPTICAL COHERENCE TOMOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN OPHTHALMOLOGY

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 - **Abstract:** Optical coherence tomography is a non-invasive method of imagining the anterior and the posterior segment of the eye. It is commonly used in ophthalmic practice to diagnose and monitor various pathologies of the eyeball. Optical coherence tomography angiography (OCTA) is a useful tool to visualize the entire retinal and choroidal microvasculature, allowing the assessment of retinal perfusion without intravenous dye administration.

Keywords: OCT, OCTA, optical coherence tomography, optical coherence tomography angiography

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INTRODUCTION

The first reports on optical coherence tomography appeared in 1990 from the laboratory of Professor James Fujimoto from Massachusetts Institute of Technology [6,7]. Optical coherence tomography (OCT) is a non-invasive imaging method based on optical scanning. It is an interferometric technique that uses near-infrared light. The principle of action of OCT is based on the interferometric measurement of the scattering or reflection of a light beam with low coherence from individual structures of the eyeball [22]. It allows the detailed assessment of the layered structure of the tissue; therefore, this method is called "in vivo optical biopsy" (see Fig. 1).

OPTICAL COHERENCE TOMOGRAPHY

In the following years, the OCT developed intensively and number of clinical publications appeared on the use of OCT in various pathologies of the anterior and posterior segment of the eye [1,3,10,12,15,17,18]. OCT is commonly used in everyday ophthalmic practice and is the most frequently ordered examination in the diagnosis of macular diseases such as age-related macular degeneration, central serous chorioretinopathy, epiretinal membrane and diabetic retinopathy (see Fig. 2 and Fig. 3).

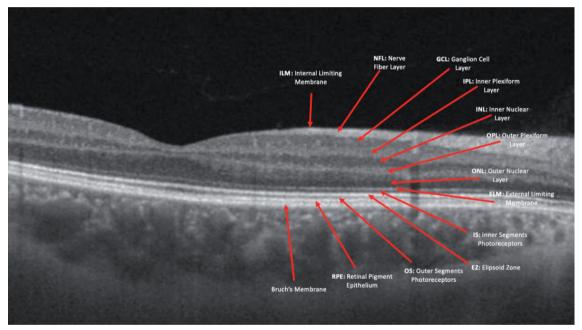


Fig. 1. Normal macula in OCT B-scan.

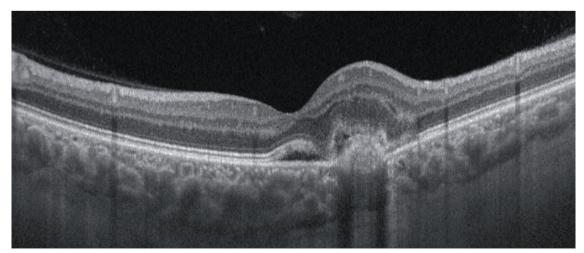


Fig. 2. OCT- B scan shows thickening of the retina, large drusen, subretinal fluid in a patient with AMD.

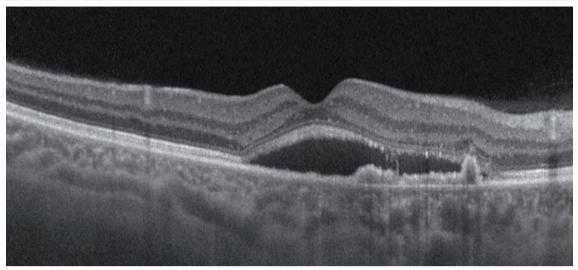


Fig. 3. OCT- B scan shows subretinal fluid in patient with central serous chorioretinopathy.

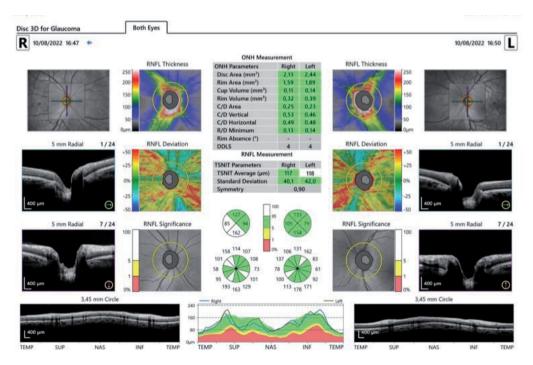


Fig. 4. OCT scan in a glaucoma patient.

Moreover, OCT is being commonly used to diagnose and monitor glaucoma patients. The examination provides assessment of the thickness of the peripapillary nerve fibers, optic disc parameters and thickness of retinal ganglion cells (see Fig. 4).

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Conventional OCT enables a detailed assessment of the structure of the retina but does not allow the assessment of the retinal circulation. Since the 1960s, fluorescein angiography (FA) has been the "gold standard" in retinal vasculature assessment [16]. This method enables visualization of even slight vascular pathologies of the posterior pole and retinal periphery. The main limitation of this technique is the necessity of intravenous dye administration (see Fig. 5).

Optical coherence tomography angiography (OCTA) is a new, non-invasive tool that delivers highly detailed, three-dimensional images of the entire microvasculature of the retina and choroid, providing retinal perfusion assessment without intravenous dye injection [14,19].

OCTA is a development of en face OCT and the latest method that allows visualization of blood



Fig. 5. Fluorescein angiography image showing normal flow in retinal vessels.

flow in the retinal vessels and choriocapillaris. Split spectrum amplitude decorrelation angiography (SSADA) is the basis of OCTA. It identifies the retinal vessels by detecting and measuring the movement of blood cells in the vessels, which allows to distinguish stationary tissue from blood flow [8]. The slowest flow that can be detected is determined by the time between consecutive Bscans. In the case of atrophy or occlusion of the vessels, the flow in the capillaries or choriocapillaris may be below the threshold of sensitivity and is then not visible on angiograms. OCTA enables a histological assessment of the vascular structure of the retina. Blood flow is visible in the superficial vascular plexus, deep vascular plexus, at the level of the outer layers of the retina and in choriocapillaris [20] (see Fig. 6).

Foveal avascular zone (FAZ) is a round capillaryfree area within the macula visualized in OCTA scans. The FAZ area in healthy eyes is measured to be about 0.26 mm2 in the superficial plexus and 0.49 mm2 in the deep vascular plexus. Measurements of the FAZ zone using OCTA have been used in patients with microcirculatory deficiency such as diabetic retinopathy. Studies reveled that the FAZ zone increase in diabetic patients (see Fig. 7).

The outer retina is avascular in the healthy eye; hence the layer is most often visible as a homogeneous, dark background (no flow). Vessels in this layer can be observed only in pathological conditions, such as the macular neovascularization (MNV) in wet age-related macular degeneration (AMD) [2]. The layer of normal choriocapillaris exposes appears as a greyish grainy background. In pathological condi-

Paczwa K. et al. - Optical coherence...

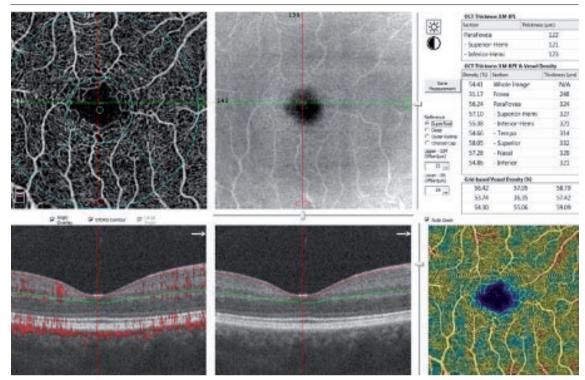


Fig. 6. OCTA assessment of the superficial retinal plexus, including detailed measurement and color map of macular vessel density.

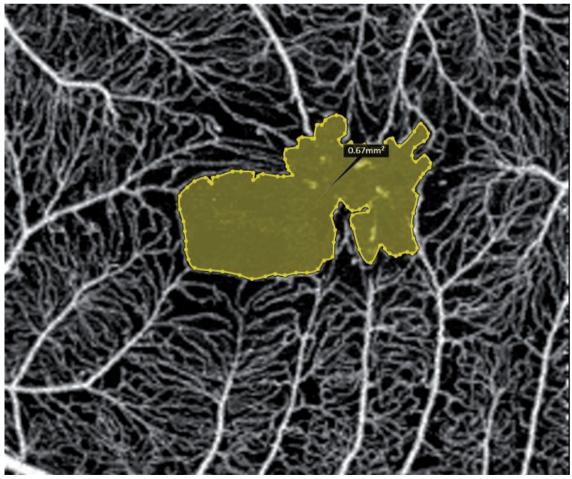


Fig. 7. OCTA showing foveal avascular zone area.

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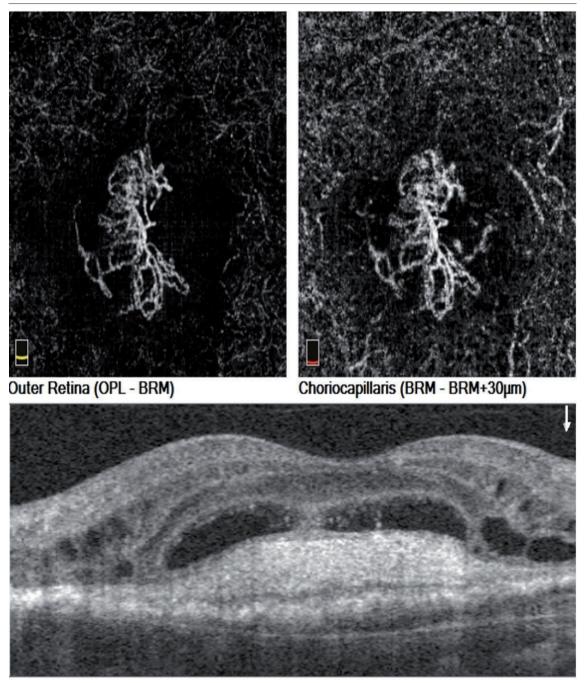


Fig. 8. OCTA image of pathological vessels at the level of outer retina (A) and choriocapillaries (B) in a patient with wet AMD. The OCT B-scan shows thickening of the retina with subretinal and intraretinal fluid and central macular neovascularization.

tions, e.g. choroidal neovascularization, abnormal flow is visible at this level (see Fig. 8).

The main indications for OCTA include agerelated macular degeneration, polypoidal choroidal vasculopathy and other causes of choroidal neovascularization such as myopia, central serous chorioretinopathy, angioid streaks and uveitis-related choroidal neovascularization. It is also a useful diagnostic tool in diabetic retinopathy, central retinal vein occlusion, central retinal artery occlusion. Furthermore, OCTA can be used in diagnostics of optic nerve pathologies for example in glaucoma [4,5,11,13]. Pathological vessels have an irregular caliber and course, form waves, bends and loops, so the blood stream may be interrupted. There may be connections between the superficial and deep weaves - shunts, rarely seen in healthy people. The background of the avascular regions is dark and smooth or slightly grainy (see Fig. 9 and Fig. 10).

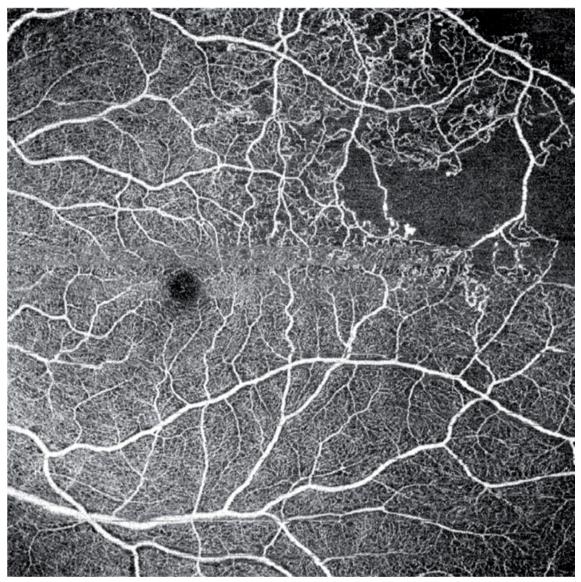


Fig. 9. OCTA image in a patient with branch retinal vein occlusion- dark areas of ischemia and irregular vessels are visible.

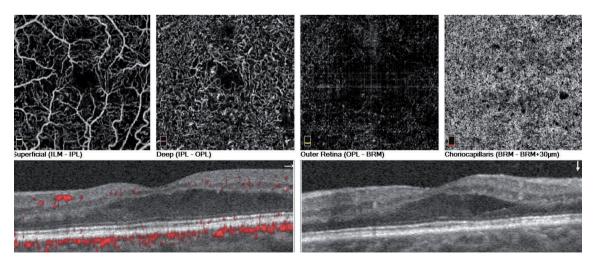


Fig. 10. OCTA image of the non-perfusion areas in superficial plexus and microaneurysms in deep vascular plexus in a diabetic patient. The OCT-B scans show thickening of the retina and intraretinal fluid.

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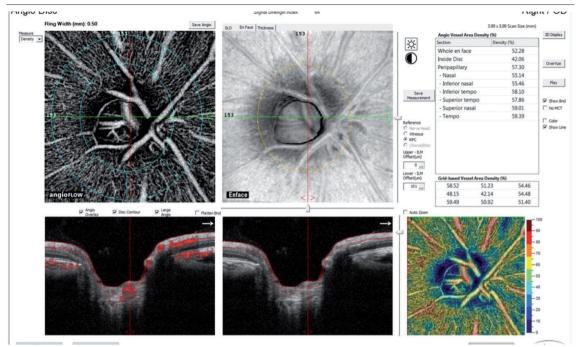


Fig. 11. The optic disc flow disturbance maybe visible even in preperimetric glaucoma.

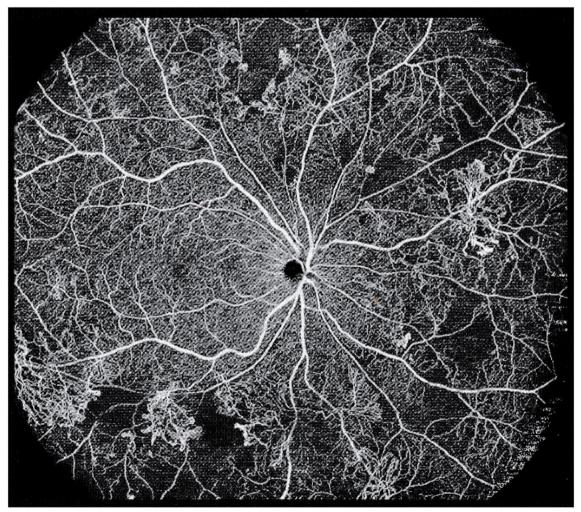


Fig. 12. Wide-field OCTA in a patient with diabetic retinopathy. (Courtesy of Prof. Hirano, MD. PhD. Shinshu Univ).

The possibility of assessing the flow in the vessels of the optic nerve, both the larger ones and the peripapillary capillaries, makes OCTA a technique more and more popular in the diagnosis of glaucoma [9] (see Fig. 11).

OCTA is a part of the routine OCT using Angio Retina scans (for macular flow assessment) or Angio Disc scans (to assess optic disc flow) and takes a few seconds.

OCTA is an irreplaceable tool used to visualize and analyze changes in capillaries and pathological vessels in retinal diseases, glaucoma and other optic nerve neuropathies.

The method limitations are the same as that of standard optical coherent tomography. These include optical media opacities, poor fixation, too narrow pupil or nystagmus.

Moreover, the limitation of typical OCTA macular scans is that it provides visualization only the area of the posterior pole. OCTA scans cannot assess leakages that are typically visualized in fluorescein angiography. Moreover, the method provides limited information about actual blood flow, imagining mainly the vascular structure. In the future we may commonly use wide-field OCTA imaging that shows peripheral vascular changes and provides a wider field of imagining [21] (see Fig. 12).

CONCLUSIONS

OCTA equals simultaneous angiography and high-resolution OCT. It enables early detection of pathologies within the vessels at different levels of the retina. OCTA as a non-invasive and repeatable test is commonly used in ophthalmology even in patients with worse cooperation.

AUTHORS' DECLARATION:

Study Design: Katarzyna Paczwa, Joanna Gołębiewska. **Data Collection:** Katarzyna Paczwa, Joanna Gołębiewska. **Manuscript Preparation:** Katarzyna Paczwa, Joanna Gołębiewska. The Authors declare that there is no conflict of interest.

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2020 | Volume 26 | Issue 4 | 57

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Acknowledgements. List all contributors who do not meet the criteria for authorship, such as technical assistants, writing assistants or head of department who provided only general support. Describe their role. Financial and other material support should be disclosed and acknowledged.

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Article with published erratum

Koffler D, Reidenberg MM. Antibodies to nuclear antigens in patients treated with procainamide or acetylprocainamide [published erratum appears in N Engl J Med 1979;302:322-5]. N Engl J Med 1979; 301:1382-5.

Article in electronic form

Drayer DE, Koffler D. Factors in the emergence of infectious diseases. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1996 Jun 5];1(1):[24 screens]. Retrieved 25 January 2013 from: http:// www.cdc.gov/ncidod/EID/eid.htm.

Electronic resource

Health on the net foundattion code of conduct (HONcode) for medical and health websites. 1997; Retrieved 9 January 2013 from https://www.hon. ch/HONcode

Article, no author given

Cancer in South Africa [editorial]. S Afr Med J 1994;84:15.

Book, personal author(s)

Lazarus RS, Folkman S. Stress, appraisal and coping. New York: Springer Publishing Co.; 1984.

Book, editor(s) as author

Norman IJ, Redfern SJ, eds. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

Book, Organization as author and publisher:

Institute of Medicine (US). Looking at the future of the Medicaid program. Washington: The Institute; 1992.

Chapter in a book

Charzewska J, Wajszczyk B, Chabrom E, Rogalska-Niedżwiedż M. Aktywność fizyczna w Polsce w rożnych grupach według wieku i płci. In: Jarosz M, ed. Otyłość, żywienie, aktywność fizyczna i zdrowie Polaków. Warszawa: Instytut Żywności i Żywienia; 2006:317-339.

Conference proceedings

Kimura J, Shibasaki H, eds. Recent advances in clinical neurophysiology. Proceedings of the 10th International Congress of EMG and Clinical Neurophysiology; 1995 Oct 15-19; Kyoto, Japan. Amsterdam: Elsevier; 1996.

Conference paper

Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, eds. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sep 6-10; Geneva, Switzerland.

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