

Assessment of effect of computer tomography with intravenous contrast administration on renal excretory function

Ocena wpływu badania tomograficznego z dożylnym podaniem kontrastu na czynność wydalniczą nerek

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ABSTRACT

INTRODUCTION: Despite the described risk of contrast-induced nephropathy, defined as sudden (up-to 48–72 h) deterioration of renal function after the administration of contrast, guidelines for border level renal excretory function markers securing safe contrast CT have not been established. The aim of study was to assess the effect of CT with intravenous contrast on changes of renal excretory function markers.

MATERIALS AND METHODS: In a prospective study, 60 patients who had CT with intravenous contrast were analyzed. Before CT and after 48 hours, the level of markers of renal function: creatinine, urea and potassium were marked in the patients' serum and the eGFR value was calculated. The patients were divided into 2 groups, depending on the output value of creatinine and eGFR: group 1 – normal values and group 2 – slightly elevated ones by 20%.

RESULTS: The average concentration of creatinine before CT did not differ significantly from the values after contrast application (1.05 ± 0.23 vs. 1.03 ± 0.26 mg/dl). The average value of eGFR before contrast CT did not differ significantly from the value after contrast application (71.53 ± 18.86 vs. 74.25 ± 22.50 ml/min./1.73 m²). No significant changes in urea and potassium concentrations after radio-contrast application were observed. The values of the analyzed markers did not differ significantly compared to the baseline values in any group, nor did sex or type of CT have an effect on the marker levels.

CONCLUSIONS: The intravenous administration of contrast during CT does not cause significant changes in renal excretory function markers, either in patients with normal renal function or in patients with baseline values elevated by 20%, irrespective of sex or type of CT.

KEY WORDS

computer tomography, radio-contrast, renal excretory function, contrast-induced nephropathy

Received: 20.03.2015

Revised: 17.04.2015

Accepted: 28.05.2015

Published online: 04.02.2016

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STRESZCZENIE

WSTĘP: Pomimo opisywanego ryzyka wystąpienia nefropatii kontrastowej definiowanej jako nagłe (do 48–72 h) pogorszenie funkcji nerek po podaniu kontrastu dotychczas nie ustalono wytycznych odnośnie do granicznego poziomu markerów czynności wydalniczej nerek, dla których dopuszczalne jest wykonanie kontrastowego badania TK. Celem pracy była ocena wpływu dożylnego podania kontrastu podczas badań TK różnego typu na zmiany wartości markerów czynności wydalniczej nerek.

MATERIAŁ I METODY: W prospektywnym badaniu analizowano 60 kolejnych pacjentów (25 kobiet i 35 mężczyzn), którym wykonano badanie TK z dożylnym podaniem kontrastu. W dniu badania oraz po 48 godzinach w surowicy pacjentów oznaczano stężenie markerów czynności nerek: kreatyniny, mocznika i potasu oraz obliczano współczynnik filtracji kłębuszkowej (eGFR). Pacjentów podzielono na 2 grupy zależnie od wyjściowych wartości badanych markerów: grupa 1 – wartości prawidłowe, grupa 2 – wartości przekraczające normę średnio o ok. 20%.

WYNIKI: Średnie stężenie kreatyniny przed badaniem nie różniło się statystycznie od stężenia po badaniu ($1,05 \pm 0,23$ vs. $1,03 \pm 0,26$ mg/dl). Średnia wartość eGFR przed badaniem nie różniła się statystycznie od wartości po badaniu ($71,53 \pm 18,86$ vs. $74,25 \pm 22,50$ ml/min./1,73 m²). Nie stwierdzono również istotnych zmian stężenia mocznika i potasu po wykonaniu badania. Wartości badanych parametrów po wykonaniu badania TK nie różniły się statystycznie w stosunku do wartości wyjściowych w żadnej grupie chorych, nie były również zależne od płci i rodzaju badania TK.

WNIOSKI: Dożylnie podanie kontrastu w trakcie badania TK nie powoduje statystycznie zmian wartości markerów czynności wydalniczej nerek u pacjentów z prawidłową czynnością nerek oraz u pacjentów z wyjściowymi wartościami markerów przekraczającymi granicę normy o ok. 20%, bez względu na płeć i rodzaj wykonanego badania.

SŁOWA KLUCZOWE

tomografia komputerowa, kontrast radiologiczny, markery czynności wydalniczej nerek, nefropatia pokontrastowa

INTRODUCTION

Acute renal failure after the application of contrast agents is defined in the literature as a sudden deterioration of renal function that occurred within 48–72 hours following the administration of a radiological contrast agent, with no other apparent reason that could cause damage to the kidneys [1,2,3]. Very often it is asymptomatic [4]. In 2005, AKIN (Acute Kidney Injury Network) proposed two separate diagnostic criteria related to the kidney damage caused by nephrotoxic agents: absolute increase in serum creatinine concentration > 0.3 mg/dl (> 26.5 mmol/l) and/or its percentage growth of 25–50% of the baseline [1,4,5,6,7] and reduced urinary incontinence < 0.5 ml/kg/h for at least 6 hours [1,5]. Acute renal failure caused by the injection of the contrast (contrast-induced acute kidney injury, CIAKI) is a factor directly damaging the kidneys as well as deteriorating long-term prognosis [8].

In 2006, the connexion between Gadolinium-based contrast media administration and the occurrence of nephrogenic systemic fibrosis (NSF) was proved [9]. The problem of the occurrence of contrast-induced nephropathy is largely underestimated, although it is the third most common nephropathy (after a decrease in renal blood flow in the course of shock and surgical intervention), and remains the most common toxic cause of acute renal failure in hospitalized patients and

accounts for about 10% of all cases of this renal failure [2,3,4,5,10,11,12].

In the general population, CIAKI risk associated with contrast administration is about 1.5%, while in patients with multiple concomitant risk factors it can be up to 50% [5]. Due to the significant increase observed in recent years in the number of radiological procedures during which a contrast agent is administered, a significant increase in the number of complications also occurs, and the incidence of acute renal failure after contrast administration causes a significant increase in patient mortality and hospitalization costs. It is estimated that 30% of patients who develop renal failure after administration of the contrast agent results in permanent renal function impairment that requires carrying out dialysis to the end of the patient's life, and in 7% of patients – death [2,3,4,7,13,14,15].

Currently, intensive research for new biomarkers that are specific and sensitive enough for the diagnosis of contrast-induced nephropathy (CIN), corresponding to the designated troponin in myocardial infarction, is being conducted [16]. So far, sufficiently extensive research enabling the elaboration of precise and unequivocal guidelines and diagnostic criteria regarding the qualifications for contrast CT scans in patients with various degrees of secretory renal function damage, including the necessity to ensure the safety of such examinations, have not been carried out [2,11,13,14].

According to ESUR (European Society of Urogenital Radiology) guidelines, the risk of NSF development

could be minimized by taking into account the distribution of contrast media into groups with the highest risk of NSF (e.g. Gadodiamid) with an intermediate risk and with the lowest risk of NSF [17,18]. It is also important to classify patients into one of 3 groups of NSF risk: at higher risk (patients in 4th and 5th stage of chronic kidney disease, with GFR < 30 ml/min.), at lower risk (patients in stage 3 of chronic kidney disease, with GFR 30–59 ml/min.) and no risk (patients with stable GFR > 60 ml/min.).

According to this classification, the risk factors of renal failure present before contrast administration should be treated: eGFR < 60 ml/min./1.73 m² before planned intra-arterial contrast administration, eGFR < 45 ml/min./1.73 m² before planned intravenous contrast administration and diagnosed or suspected acute renal failure. Those risk factors could be enhanced in connexion with numerous concomitant diseases, age and taking nephrotoxic drugs. Before planned CT examination, patients with increased NSF risk should be identified in order to determine eGFR before and within 7 days after contrast administration, especially those with previously determined eGFR < 60 ml/min./1.73 m², with planned intra-arterial contrast administration, aged > 70 years and with concomitant diseases: renal disease, renal surgery, proteinuria, diabetes mellitus, hypertension, gout and recent nephrotoxic drug taking [17,18].

The aim of the study was to assess the effect of intravenous administration of contrast during various types of computed tomography examinations on changes in the values of selected markers of renal excretory function, routinely assayed in the qualifications for these examinations, in patients with normal and mildly impaired renal secretory function.

MATERIAL AND METHODS

The following 60 patients participated in a prospective study: 25 women (41.7%) and 35 men (58.3%), aged from 32 to 89 years, hospitalized in the period from 17.10.2013 to 02.20.2014 in the Department of Internal Medicine, Angiology and Physical Medicine of Specialistic Hospital No. 2 in Bytom in order to conduct in the Department of Radiology at the Hospital a computed tomography examination with intravenous contrast administration for various indications.

The study excluded patients with allergies to radiographic contrast, chronic renal failure or other health conditions which may cause a renal excretory function disorder. The mean age of the examined patients was 65.1 ± 13.0 years – in women 68.1 ± 13.1 years and in men 62.9 ± 12.65 years. During

the dynamic CT examinations, performed due to planned indications, intravenous nonionic radiographic contrast Omnipaque was administered to the patients. The average volume of contrast during CT of the abdomen and pelvis was 75.3 ± 15.1 ml, during CT of the chest it was 70.6 ± 9.8 ml, and during CT of the head it was 40.0 ± 0.0 ml. In turn, the volume of contrast during CT angiography was in the range of 100 to 120 ml (average 115.9 ± 4.4 ml). Table I shows the type and number of particular CT examinations performed

Table I. Type and number of contrast computer tomography scans
Tabela I. Rodzaj i liczba wykonanych tomograficznych badań kontrastowych

Total number of CT exams with contrast administration (60)	
CT of internal organs (43)	CT angiography (17)
• CT of abdomen and pelvis (33)	• CT angiography of the pulmonary arteries (6)
• CT of chest (8)	• CT angiography of the iliac arteries and lower limbs (8)
• CT of head (2)	• CT angiography of the abdominal aorta and its branches (2)
	• CT angiography of the carotid and vertebral arteries (1)

Before the CT scan with intravenous contrast, and 48 hours after the end of the examination, 10 ml of blood was collected in polypropylene syringes with a closed vacuum system containing a coagulation activator. Then, after decantation and centrifugation of the blood samples, selected markers of renal excretory function were determined in the obtained serum with use of routine laboratory methods: serum creatinine, urea and potassium concentration, and the glomerular filtration rate (eGFR) was calculated. Depending on the output values of the studied markers of renal excretory function: serum creatinine levels and eGFR, the patients were divided into two groups – the first group with normal renal excretory function and the second group with a slight impairment of excretory function. In 46 patients from Group 1, the output values of these two markers were within normal laboratory limits: 0.4–1.24 mg/dL for creatinine and for eGFR > 60 ml/min./1.73 m², respectively, whereas in 14 patients from Group 2 the output values of these markers exceeded the normal laboratory limits by approximately 20%.

The results obtained in both groups, presented as mean ± standard deviation were statistically analyzed using the computer program STATISTICA for Windows version 10.0 (StatSoft, Krakow, Poland). Compliance of the distribution of the variables with normal distribution were tested by means of the Shapiro-Wilk test, and the statistical significance of the differences between the values of particular markers before and after the CT scan examination was estimated by means of Student's t test for paired data. P values < 0.05 were considered to be statistically significant.

RESULTS

The mean values of renal excretory function markers in the whole group of examined patients with regard to sex, measured before and 48 hours after contrast CT scan are shown in Table II.

The mean serum concentration of creatinine and mean value of eGFR 48 hours after intravenous administration of contrast were: 1.03 ± 0.26 mg/l and 74.25 ± 22.50 ml/min./1.73 m², respectively, and they did not differ significantly from the values noted prior to the CT scan (1.05 ± 0.23 mg/dl and 71.53 ± 18.86 ml/min./1.73 m², respectively). The serum concentration of urea and potassium 48 hours after intravenous administration of contrast did not differ significantly from the baseline values of those markers determined prior to the CT scan either.

As shown in Table II, the sex of the patients had no significant impact on the occurrence of significant changes in the value of any of the analyzed markers of renal excretory function. A significant increase in

serum creatinine after the administration of contrast, to a level exceeding the upper limit of the standard by 18%, was noted only in one patient in which the level of this marker before the CT scan was within normal laboratory limits.

The average values of renal excretory function markers in patients with normal renal excretory function with regard to sex, measured before and 48 hours after contrast CT scan are shown in Table III.

In this group of patients, similar to the analysis carried out overall for all the examined patients, 48 hours after intravenous administration of contrast, no statistically significant changes in the values of any of the assessed markers of renal excretory function were found as compared to the baseline values prior to the CT scan. Also in this case, the sex of the patients had no significant impact on the values of the analyzed markers. The average values of renal excretory function markers in the group of patients with slightly impaired renal excretory function, with regard to sex, measured before and 48 hours after the contrast CT scan are shown in Table IV.

Table II. Comparison of renal excretory function marker values (mean \pm SD) before and after contrast tomography scan in whole group of examined patients with regard to sex ($p > 0.05$)

Tabela II. Porównanie wartości markerów czynności wydalniczej nerek (średnia \pm SD) przed i po tomograficznym badaniu kontrastowym w całej grupie badanych pacjentów, z uwzględnieniem płci ($p > 0,05$)

Markers	Total		Women		Men	
	before CT scan	after CT scan	before CT scan	after CT scan	before CT scan	after CT scan
Creatinine [mg/dl]	1.05 ± 0.23	1.03 ± 0.26	0.97 ± 0.23	0.97 ± 0.26	1.10 ± 0.22	1.08 ± 0.25
eGFR [ml/min./1,73 m ²]	71.53 ± 18.86	74.25 ± 22.50	64.72 ± 15.75	66.60 ± 20.25	76.40 ± 19.58	79.71 ± 22.71
Urea [mg/dl]	34.82 ± 15.83	31.28 ± 12.34	33.97 ± 14.00	31.99 ± 12.87	35.53 ± 17.25	30.74 ± 11.90
Potassium [mmol/l]	4.31 ± 0.53	4.30 ± 0.53	4.19 ± 0.52	4.10 ± 0.66	4.40 ± 0.53	4.46 ± 0.46

Table III. Comparison of renal excretory function marker values (mean \pm SD) before and after contrast tomography scan in group of patients with normal renal excretory function, with regard to sex ($p > 0.05$)

Tabela III. Porównanie wartości markerów czynności wydalniczej nerek (średnia \pm SD) przed i po tomograficznym badaniu kontrastowym w grupie pacjentów z prawidłową czynnością wydalniczą nerek, z uwzględnieniem płci ($p > 0,05$)

Markers	Total		Women		Men	
	before CT scan	after CT scan	before CT scan	after CT scan	before CT scan	after CT scan
Creatinine [mg/dl]	0.97 ± 0.15	0.96 ± 0.22	0.91 ± 0.14	0.90 ± 0.27	1.02 ± 0.14	1.00 ± 0.20
eGFR [ml/min./1,73 m ²]	77.75 ± 15.39	80.46 ± 20.36	73.41 ± 9.31	75.18 ± 17.55	80.13 ± 17.56	83.35 ± 21.45
Urea [mg/dl]	29.64 ± 7.87	27.42 ± 8.13	29.13 ± 5.31	27.67 ± 7.16	30.04 ± 9.38	27.23 ± 8.90
Potassium [mmol/l]	4.29 ± 0.53	4.36 ± 0.39	4.15 ± 0.52	4.29 ± 0.38	4.41 ± 0.54	4.39 ± 0.41

Table IV. Comparison of renal excretory function marker values (mean \pm SD) before and after contrast tomography scan in group of patients with slightly impaired renal excretory function, with regard to sex ($p > 0.05$)

Tabela IV. Porównanie wartości markerów czynności wydalniczej nerek (średnia \pm SD) przed i po tomograficznym badaniu kontrastowym w grupie pacjentów z nieznacznie upośledzoną czynnością wydalniczą nerek, z uwzględnieniem płci ($p > 0,05$)

Markers	Total		Women		Men	
	before CT scan	after CT scan	before CT scan	after CT scan	before CT scan	after CT scan
Creatinine [mg/dl]	1.47 ± 0.12	1.43 ± 0.17	1.46 ± 0.09	1.43 ± 0.21	1.47 ± 0.14	1.43 ± 0.13
eGFR [ml/min./1,73 m ²]	46.67 ± 7.24	49.42 ± 10.26	46.25 ± 8.33	48.48 ± 11.18	47.50 ± 2.38	51.50 ± 5.72
Urea [mg/dl]	58.17 ± 21.27	48.67 ± 14.57	53.33 ± 20.43	49.03 ± 17.14	63.00 ± 20.99	48.30 ± 9.12
Potassium [mmol/l]	4.31 ± 0.52	4.12 ± 0.89	4.32 ± 0.57	3.73 ± 0.74	4.30 ± 0.52	4.53 ± 0.57

Also in this group of patients, the mean values determined 48 hours after intravenous administration of contrast did not differ significantly from the baseline values determined prior to the CT scan of any of the markers of renal excretory function. Also in this case, the sex of patients had no significant impact on the level of the analyzed markers.

The amount of intravenous contrast administered during the CT scan did not have any significant effect on the values of renal excretory function markers. In the case of tomographic studies of the internal organs, the average serum concentration of creatinine and mean value of eGFR 48 hours after intravenous contrast administration were: 0.97 ± 0.21 mg/dl and 78.95 ± 21.56 ml/min./ 1.73 m², respectively, and they did not differ significantly from the baseline values (1.0 ± 0.19 mg/dl and 75.35 ± 18.25 ml/min./ 1.73 m², respectively). Similarly, in the case of vascular studies (angiography), requiring nearly half a larger volume of contrast, the average serum concentration of creatinine and mean value of eGFR 48 hours after the administration of contrast were: 1.18 ± 0.31 mg/dl and 62.35 ± 20.91 ml/min./ 1.73 m², not differing significantly from the baseline values either (1.17 ± 0.29 mg/dl and 61.88 ± 17.29 ml/min./ 1.73 m², respectively).

DISCUSSION

Nephropathy after the application of contrast agents during invasive procedures and during an intravenous contrast CT scan is an iatrogenic complication, that, in the opinion of some authors, is becoming an increasingly common clinical problem [5,11]. The results of this study indicate that the administration of a routine radiological contrast dose during a CT scan does not result in statistically significant renal excretory dysfunction, neither in the group of patients with normal renal function, nor in the group of patients with slightly impaired excretory function of this organ, regardless of gender or the type of CT scan examination performed. It seems that the relatively higher incidence of contrast-induced nephropathy observed in other studies [2,3,4,5,10,11,12] can result from a more liberal eligibility for the contrast CT scan examination or longer observation time after the CT scan was performed.

Knowledge of the pathogenesis of CIAKI and appropriate preventive treatment can protect patients from the severe consequences of contrast-induced nephropathy [5]. Numerous publications on contrast-induced nephropathy indicate the importance of procedures such as: appropriate preparation of the patient for the examination, the correct type of contrast agent used during diagnostic procedures and proper treatment

after completion of the examination. CIAKI pathogenesis is complex, and the share of individual mechanisms, often overlapping, in the formation of contrast-induced nephropathy has not been yet clearly defined. Currently, among those pathomechanisms the following are mentioned: ischemic renal damage, direct toxic effect of the contrast, intrarenal arteriolar spasm, hypoxia of glomeruli and immune responses [4].

It is generally accepted that the main cause of contrast-induced nephropathy is the output loss of glomerular filtration efficiency, so it seems appropriate to control the serum creatinine level before each test. The level of serum creatinine within laboratory limits is related with a slight threat of nephropathy and allows one to maintain a safe margin of error for contrast administration [13]. Most of the publications confirmed that the incidence of acute renal insufficiency significantly increased when the patient's GFR is less than 60 ml/min./ 1.73 m², which normally corresponds to the serum concentration of creatinine 1.5 mg/dl (taking into account the fact that the value of serum creatinine does not accurately reflect the full extent of creatinine clearance and intensity of renal damage, because with patient age the physiological loss of glomeruli of the kidneys occurs, which is inextricably linked with an increase in the creatinine serum level) [2,3,5]. In some cases, even a slight increase in the creatinine serum level may precede a significant deterioration of renal function, especially if the baseline values of this marker remained within normal limits [19]. Moreover, in many cases, an increase in the serum creatinine level after the administration of contrast reaches its peak between 5 and 7 days, and then returns to a normal level within 10 days after contrast administration [3,6,19,20,21].

Among other pathomechanisms of CIAKI, also the effect of the contrast agent on the vascular-shrink of arterioles in the core and kidney cortex, caused by adenosine generated by the hydrolysis of ATP, should be considered (adenosine has a strong vascular shrink effect on muscle afferent arterioles via A1 receptors and on muscle dilator efferent arterioles via A2 receptors, causing a significant decrease in renal blood flow) [5,12,21]. Recently the hypothesis that renal tubular obstruction is caused by precipitating oxalate, urate and proteins with different molecular weight is also taken into account [12]. Finally, some authors suggest that impaired microcirculation in the renal core and cortex is created by changes in the physicochemical properties of the blood caused by the administration of contrast agents, which increase blood viscosity and as a consequence decrease its flow in the kidneys [21].

In the process of qualifying the patient for a CT scan with intravenous contrast administration, additional co-morbidities and pathological conditions which are risk factors of CIAKI (shown in Table V) must

Table V. Risk factors of contrast-induced nephropathy
Tabela V. Czynniki ryzyka wystąpienia nefropatii kontrastowej

Patient factors		Procedure factors		Modifyable factors	
1.	Previously existing renal failure, especially due to diabetic nephropathy	1.	Subsequent exposure to contrast agents in < 72 hours	1.	Osmolality and ionicity of contrast agent
2.	Chronic heart failure	2.	High-osmolality contrast	2.	Volume and multiplicity of contrast administration
3.	Diabetes	3.	Large amount of administered contrast	3.	Dehydration
4.	Reduced left ventricular ejection fraction	4.	Intra-arterial administration of contrast	4.	Acute coronary syndrome within 24 hours prior to angiography
5.	Hypotension			5.	Hypotony
6.	Chronic liver failure				
7.	Patient age (> 70 years)				
8.	Drugs (NSAIDs, ACE inhibitors, furosemide, aminoglycosides)				
9.	Hypoalbuminemia (< 3.5 g/l)				
10.	Decreased hematocrit value (< 36% for F, < 39% for M)				

Table VI. Classification of radio-contrasts
Tabela VI. Podział radiologicznych środków kontrastowych

I GENERATION	High-osmolal (1400–1800 mosmol/kg), ionic monomers
II GENERATION	Low-osmolal (500–850 mosmol/kg), nonionic monomers
III GENERATION	Iso-osmolal (290 mosmol/kg), non-ionic dimers

be considered, as the presence of three or more of risk factors increases the likelihood of CIAKI occurrence almost 3-fold [16].

Differentiating the causes of renal excretory function deterioration in patients after the administration of contrast, the time relation between the occurrence of that pathology and the administration of the contrast should be estimated and in the case of lack of evidence for the existence of a typical dependence, other causes of an acute renal failure occurrence should be considered, such as: cholesterol embolism, renal artery embolism or the use of drugs that affect the renin-angiotensin-aldosterone system [2,12].

In the prevention of CIN it is very important to choose the right type of administered contrast agent, which requires knowledge on its toxicity and probability of creating an allergic reaction or other side effects [12]. Table VI presents the characteristics of currently used radiographic contrast agents, of which potentially the safest, from the point of view of the risk of contrast-induced nephropathy, are the third-generation agents.

Although the results presented in this study did not confirm the significant impact of the type of CT scan performed (and indirectly the volume of administered contrast) on the value of renal excretory function markers, the potential effect of the volume of contrast

agent administered on the development of contrast-induced nephropathy has to be kept in mind [21]. Currently, the maximum allowable dose of contrast is usually calculated using the following formula: MRDC (maximal allowed radio-contrast dose) = 5 ml of contrast agent x body weight [kg]/serum creatinine [mg/dl] [21].

It has been proved that proper hydration before a contrast examination increases renal blood flow and glomerular filtration, resulting in a reduction in negative hemodynamic effects, and reduces the likelihood of CIN occurrence [6,7]. Therefore, according to experts, before and after a CT scan with intravenous contrast administration, adequate hydration is recommended [5]. This procedure is so far the only proven method for reducing the risk of CIN [21].

CONCLUSIONS

The intravenous administration of contrast during CT scans does not cause significant changes in the values of renal excretory function markers, either in patients with initially normal renal function or in patients with baseline values slightly exceeding the normal marker limits by approx. 20%, regardless of sex or type of CT scan examination conducted.

Author's contribution

Study design – M. Pietrzak, G. Cieślak
 Data collection – M. Pietrzak
 Data interpretation – M. Pietrzak, G. Cieślak
 Statistical analysis – M. Pietrzak, G. Cieślak
 Manuscript preparation – M. Pietrzak, G. Cieślak
 Literature research – M. Pietrzak, G. Cieślak

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