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Frequency of the malignant neoplasms in population commencing renal replacement therapy (RRT) in the years 2001-2015 – one-unit experience

Częstość nowotworów złośliwych w populacji rozpoczynającej leczenie nerkozastępcze w latach 2001-2015 w doświadczeniu jednego ośrodka

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Keywords

renal failure, renal replacement therapy (RRT), neoplasms, multiple myeloma

Słowa kluczowe

niewydolność nerek, leczenie nerkozastępcze, nowotwory, szpiczak mnogi

Summary

Introduction. The incidence of malignant neoplasms in population of patients initiating renal replacement therapy (RRT) is rising last years, which is related to the aging of general population and to the increasing availability of renal replacement therapy to renal patients, including those with neoplastic diseases.

Aim. The aim of this work was to analyse the frequency of malignant neoplasms in the group of patients starting renal replacement therapy.

Material and methods. The retrospective analysis of the medical records in years 2001-2015 at the Dialysis Unit in the Priest J. Popiełuszko Bielański Hospital in Warsaw.

Results. The RRT was started in 669 patients (F-270, M-399) and 84 of them (12.5%) had malignant neoplasm at the RRT start. The largest group – 23 persons (27.4%) were patients with the neoplasm of lymphatic system, most of them with multiple myeloma.

Conclusions. The incidence of malignancies at the commencing of chronic RRT in the 669 consecutive patients at our dialysis unit, was 12.5%, in this the malignancies of lymphatic system were 3.4% (23/669) – 3.3% (9/270) and 3.5% (14/399) in woman and man, respectively.

Streszczenie

Wstęp. Częstość nowotworów złośliwych w populacji pacjentów rozpoczynających leczenie nerkozastępcze zwiększa się w ostatnich latach, co jest związane ze starzeniem się populacji ogólnej i rosnącą dostępnością leczenia nerkozastępczego, także dla osób z chorobą nowotworową.

Cel pracy. Celem niniejszego opracowania była analiza częstości nowotworów złośliwych w grupie pacjentów rozpoczynających leczenie nerkozastępcze.

Materiał i metody. Przeprowadzono retrospektywną analizę historii chorób wszystkich pacjentów, którzy w latach 2001-2015 rozpoczęli leczenie w Ośrodku Dializ przy Szpitalu Bielańskim im. ks. J. Popiełuszki w Warszawie.

Wyniki. Leczenie nerkozastępcze rozpoczęło 669 pacjentów (K-270, M-399), a 84 z nich miało nowotwór złośliwy w chwili rozpoczynania leczenia nerkozastępczego. Największą grupę – 23 osoby (27,4%), stanowili pacjenci z nowotworem układu chłonnego, w większości ze szpiczakiem mnogim.

Wnioski. Częstość choroby nowotworowej u 669 kolejnych pacjentów, którzy rozpoczęli leczenie nerkozastępcze w naszej stacji dializ, wyniosła 12,5%, w tym nowotwory układu chłonnego odpowiadały za 3,4% (23/669) – odpowiednio 3,3% (9/270) oraz 3,5% (14/399) u kobiet i mężczyzn.

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INTRODUCTION

Malignant neoplasms are among the most frequent causes of morbidity and mortality in general popula-

tion. Not so long ago the evident neoplastic disease excluded inclusion into chronic RRT program. The situation was changed during the last years and now only the advanced, disseminated neoplastic disease may serve as a reason for refusing this therapy (1). In patients presenting with renal failure, as well as in the dialyzed ones, the neoplasms frequency is higher than in general population and is rising throughout the last decades (1-3). This is caused by the malfunction of the immunological system due to uremic state and to the prolonged exposure to uremic toxins. Simultaneously, the aging population and the progress in treatment of other diseases (cardiosurgery, vascular surgery, effective treatment of metabolic and vascular diseases) allow for registering new patients with neoplastic diseases into the group of persons beginning the RRT - these patients simply live long enough, to develop, and present with neoplastic disease at the beginning of RRT. A different problem would be the group of patient for whom the relation between appearance of the neoplasm and the necessity to initiate RRT is strictly related to a specific effect of neoplasm, e.g. infiltration of the urinary tract by a tumor - like in the obstructive nephropathy, or like in myeloma nephropathy. In this group a deterioration of kidney function (acute or chronic) may cause a necessity of initiating the RRT also independently. Many medical reports confirm the huge frequency of malignant neoplasms in the population of haemodialysed patients (2-6), and the increasing incidence of neoplastic diseases in patients with chronic renal failure and during RRT (2, 3, 5). In some of these patients the developing neoplasm may induce the uremic state demanding RRT. That would be in cases of obstructive nephropathy caused mainly by infiltration of the urinary tract by cancers of prostate, uterus, bladder or kidney. Also, many patients with haematological diseases develop severe uremic condition demanding RRT, which is on the one hand strictly bound to the specificity of haematological disorder (e.g. myeloma nephropathy or glomerulopathies in lymphatic system diseases) (7-9), and on the other hand with the specificity of the therapy (nephrotoxic effect of chemotherapy, higher incidence of AKI because of prerenal causes) (7-9).

AIM

The goal of the study was to analyze the incidence of malignant neoplasms in the group of patients beginning renal replacement therapy (RRT).

MATERIAL AND METHODS

This is a retrospective observational study based on the analysis of patients' medical records. All patients commencing RRT in the years 2001-2015 (till June) at the Dialysis Unit DIAVERUM in Warsaw, Ceglowska Street 80 (previously Non-Public Health Care Centre "Dialysis and Diagnostics Centre"), at the Priest J. Popiełuszko Bielański Hospital in Warsaw, were analyzed. In every patient with neoplastic disease in anamnesis or diagnosed at the moment of qualification to RRT, the decision on initiating the RRT was done individually, based on clinical and biochemical indications, and taking into account the good general condition (despite neoplastic disease), the forecasted surviving time, and with an intention of delivering the optimal therapy, especially to minimize side effects and patient's suffering, and avoiding the futile therapy.

RESULTS

In years 20012-2015 (till June, 30) 653 adult patients initiated the chronic RRT. The dialysis was also performed in 16 patients presenting with acute kidney injury related to the neoplastic disease. Out of these 669 patients (270 females and 399 men) 72 (12.5%) were diagnosed with neoplastic disease time and/or cause-related with the beginning of RRT, and 12 had the diagnosis made beforehand - 8 (75%) initiated RRT with the relapse of neoplastic disease, (including 1 in the dissemination phase of disease), 4 (25%) had a new neoplasm. Two neoplasms in one patient were diagnosed in 8 patients: 4 patients with existing cancer were diagnosed with another one (patients with bladder cancer had new diagnosis of kidney cancer), and 4 developed new cancer with no relapse of the one diagnosed in the past.

Thus, the total number of cancers diagnosed in 84 patients commencing RRT was 92 (80 newly diagnosed, 8 protracted, and 4 successfully treated), but only 88 were considered active at RRT initiation and analysed (fig. 1). Table 1 presents the neoplastic past of patients beginning RRT with an active neoplastic disease.



Fig. 1. Appearance of the old-diagnosed and new-diagnosed neoplasms during reviewed time 2001-2015.

In 12 patients beginning RRT with an active neoplastic disease and with the neoplasm diagnosed in the past (jointly) – the most common, in 6 cases (50%) were cancers of the urinary tract: 4 cancers of the kidney and 2 cancers of the bladder. The time between the diagnosis and the relapse did not exceed 5 years in 5 out of 8 patients, and exceeded it in 3.

The 84 patients beginning RRT with active neoplastic disease had 88 different neoplasms (tab. 2). The 72 patients (85.7%) had no neoplasm history (first diagnosis of neoplasm), but in 4 of them (4.8% of all analyzed) two independent neoplasms were diagnosed at the same time.

Patients with multiple myeloma and other lymphomas were the biggest group in patients beginning RRT with coexisting neoplastic disease – 23 persons (27.4%), and the percentage was almost the same

Past neoplasm	n	Time from diagnosis of the neoplasm to RRT (months)	Relapse (number of p-ts)	No relapse (number of p-ts)	de novo (diagnosis)
Bladder cancer	2	25-70	2		
Renal cancer	4	48-197	3	1	Urothelial kidney cancer (contralateral kidney, after 197 months)*
Brest cancer	1	36	1		
Lung carcinoma	1	192		1	Hodgkin's lymphoma*
Uterine cancer	2	20-252	1	1	Kidney cancer*
Colorectal cancer	1	45	1		
Mandibular cancer	1	228		1	Multiple myeloma*
Total	12	20-252	8	4	

Table 1. Neoplastic past of the patients beginning RRT with an active ne	oplastic disease	(2001 - 2015)
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*Cases with new neoplasm and no relapse of the first one

Table 2. Neoplasms in patients beginning RRT with an active neoplastic disease (2001-2015).

First (n = 72) or relapse (n = 8) neoplasm	Total neoplasms (n)	Newly diagnosed neoplasms (n)	Coexisting with a second neoplasm (n)	Relapse of the past neoplasm (n)
Multiple myelomas and other lymphomas (together): multiple myeloma other lymphomas	23 20 3	23 20 3	2	0
Carcinomas of the urinary tract (together): carcinoma of the bladder carcinoma of the kidney	25 9 16	20 7 13	6 4	5 2 3
Prostate cancer (together)	20	20	4	
Other (together)	20	17		3
Carcinoma of the uterus	5	4		1
Colorectal carcinoma	4	3		1
Carcinoma of the lungs	2	2		
Cholangiocarcinoma	2	2		
Breast carcinoma	1	-		1
Ovarian carcinoma	1	1		
Carcinoma with non-specified onset	2	2		
Melanoma malignum	1	1		
Polycythaemia vera	1	1		
Pheochromocytoma	1	1		
Total	88	80*	8 p-ts with 2 neoplasms	8

*72 patients with 1 new cancer + 4 with new cancer with no relapse of the old one + 4 with two new cancers

for woman and man (3.3% - 9/270 vs 3.5% - 14/399). The next two groups comprised patients with cancers of the urinary tract (cancers of the kidney and cancers of the bladder) - 21 persons (25%) and with prostate cancer- 20 persons (23.8%). It seems worth mentioning that 4 patients with cancer of the prostate had coexisting cancers of the bladder (2 cases) or multiple myeloma (2 cases), and 4 other patients, with bladder cancer had coexisting kidney cancer.

DISCUSSION

The population under study comprises of both, patients starting haemodialysis for chronic kidney disease and for acute kidney injury. Due to the nature of the neoplasm in no patient presenting with AKI and neoplasm the withdrawal of dialysis therapy was expected. This warranted the merging of this tiny subpopulation with the vast majority of CRF patients. No patient in our group started dialysis second to tumor lysis syndrome or hypercalcemic crisis – all AKI cases resulted from the surgically-untreatable causes. Multiple myeloma incidence ranges 4-5 cases per 100 000 yearly, and increases along the age of patient (7). Typical myeloma nephropathy may cause renal failure in 90% of patients with myeloma (10). On the other hand, patients with myeloma form 1-2% pool of haemodialysed patients (11). In this point our results are not different from the published data. In our study in the 669 patients beginning RRT there were 23 patients with neoplasms of the lymphatic system (3.4%). It is worth remember-

ing, that the simultaneous appearance of neoplasm together with uremic state demanding RRT very frequently would be caused by the fact, that the neoplastic disease is revealed in aged individuals presenting with many co-morbidities, including the vascular or metabolic ones. Our data confirm the high incidence of neoplasms in patients requiring RRT with no other contraindication to start it. This was observed in every eighth patient (12.5%) at our unit. This is more than double of that reported in Poland (5.7%) in a large multicenter cohort of 5648 patients on haemodialysis in 2002-2003. The majority of our patients commenced dialysis only after the Sydor et al. study had been completed, and the difference most probably reflects jointly the changing, more liberal acceptance to dialysis and the rising incidence of neoplasms in patients with advanced renal disease (12). In our population the majority of patients presented with multiple myeloma or genitourinary system tumors, which confirms the previous observation of Rosa et al. in patients in need of

BIBLIOGRAPHY

- Pippias M, Jager KJ, Kramer A et al.: The changing trends and outcomes in renal replacement therapy: data from the ERA-EDTA Registry. Nephrol Dial Transplant 2015. doi: 10.1093/ndt/gfv327.
- Maisonneuve P, Agodoa L, Gellert R et al.: Cancer in patients on dialysis for end-stage renal disease: an international collaborative study. Lancet 1999; 354: 93-99.
- 3. Stengel B: Chronic kidney disease and cancer: a troubling connection. J Nephrol 2010; 23: 253-262.
- 4. Vajdic CM, McDonald SP, McCredie MR et al.: Cancer incidence before and after kidney transplantation. JAMA 2006; 296: 2823-2831.
- Butler AM, Olshan AF, Kshirsagar AV et al.: Cancer incidence amoung US medicare ESRD receiving hemodialysis 1996-2009. Am J Kid Dis 2015; 65(5): 763-772.
- Lin HF, Li YH, Wang CH et al.: Increased risk of cancer in chronic dialysis patients: a population-based cohort study in Taiwan. Nephrol Dial Transplant 2012; 27: 1585-1590.
- 7. Rajkumar SV: Multiple myeloma: 2012 update of diagnosis, risk-stratification, and management. Am J Hematol 2012; 87: 79-88.

dialysis due to AKI (13). Thus, our population seems to mirror that of Poland and one might conclude that the pattern of neoplasms in advanced renal failure remains stable in the last two decades, despite the increasing neoplasm incidence.

CONCLUSIONS

- 1. The most common malignant neoplasms in the group of patients with advanced uremic state demanding RRT were neoplasms of the lymphatic system (predominantly multiple myeloma), which were present in 26.1% (23/88) of all cases with neoplasms and in 3.4% of all patients beginning RRT.
- 2. Carcinomas of the urinary tract (carcinoma of the kidney or of the bladder) and prostate carcinoma, were equally frequent, each were present in 23.8% (20/88) of all cases with neoplasms, which makes 3% of all patients beginning RRT.
- Dimopoulos MA, Terpos E: Renal insufficiency and failure. Hematology Am Soc Hematol Educ Program 2010; 2010: 431-436.
- Charliński G, Ostrowski G, Wiater E: Leki immunomodulujące oraz inhibitory proteasomów w leczeniu chorych na szpiczaka plazmocytowego z niewydolnością nerek. Acta Haematol Pol 2012; 43: 173-186.
- 10. Herrera GA, Senders PW: Paraproteinemic renal disease that involve the tubule-intestitium. Contrib Nephrol 2007; 153: 105-115.
- Tsakiris DJ, Stel VS, Finne P et al.: Incidence and outcome of patients starting renal replacement therapy for end-stage renal disease due to multiple myeloma or ligh-chain deposit disease: an ERA-EDTA Registry study. Nephrol Dial Transplant 2010; 25(4): 1200-1206.
- Sydor A, Czapkowicz-Gryszkiewicz L, Didkowska J et al.: Nowotwory złośliwe u chorych z przewlekłą niewydolnością nerek. Problemy Lekarskie 2006; 45(3): 159-160.
- Rosa J, Sydor A, Sułowicz W: Rokowanie u chorych z ostrym uszkodzeniem nerek w przebiegu nowotworów złośliwych. Przegląd Lekarski 2014; 71(2): 72-77.

received/otrzymano: 02.09.2015 accepted/zaakceptowano: 26.09.2015