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Life span and outcomes in patients with malignant neoplasms commencing renal replacement therapy (RRT) in the years 2001-2015 – one-centre experience

Długość życia i losy pacjentów z nowotworami złośliwymi rozpoczynających leczenie nerkozastępcze w latach 2001-2015 w doświadczeniu jednego ośrodka

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Keywords

dialysis, neoplasm, life span, multiple myeloma

Słowa kluczowe

dializa, nowotwór, długość życia, szpiczak mnogi

S u m m a r y

Introduction. The growing availability of renal replacement therapy (RRT) may rise the incidence of malignant neoplasms at commencement of chronic dialysis. The prognosis for such patients has not been studied extensively.

Aim. To analyse the life span and outcomes of patients commencing RRT with a co-existing malignant neoplasm. The secondary aim was to analyse the causes of death in this population.

Material and methods. The retrospective search of medical records from years 2001-2015 at the Diaverum Dialysis Unit (former Non-Public Health Care Unit "Centre of Dialysis and Diagnostics") at the Priest J. Popiełuszko Bielański Hospital in Warsaw.

Results. Out of the 669 patients (F-270, M-399) who commenced chronic RRT (intention to treat) during the 174 months analysed, 84 (12.5%) had malignant neoplasm time- and/or cause-related to the RRT commencement. The outcomes were available in 64 patients on HD at the end of observation (20 patients were lost to follow-up – 5 discontinued HD, 5 partly recovered renal function, and 10 moved to another unit). Died 57 patients on the chronic haemodialysis therapy program (HD), 1 has been transplanted, and 6 continued the treatment started 1-84 months earlier.

Conclusions. Chronic haemodialysis should be initiated also in patients presenting with neoplastic disease whenever the indications to that treatment exist. In these patients the life expectancy can be quite long.

S t r e s z c z e n i e

Wstęp. Rosnąca dostępność leczenia nerkozastępczego może powodować wzrost częstości nowotworów złośliwych u pacjentów rozpoczynających to leczenie. Losy pacjentów z nowotworem rozpoczynających program przewlekłymi dializami nie były do-tychczas wystarczająco analizowane.

Cel pracy. Analiza długości życia i losów pacjentów z nowotworami złośliwymi rozpoczynających leczenie nerkozastępcze. Dodatkowym celem była analiza przyczyn zgonów u tych chorych.

Materiał i metody. Przeprowadzono retrospektywną analizę zgromadzonej dokumentacji medycznej wszystkich pacjentów rozpoczynających w latach 2001-2015 (do 30 czerwca) leczenie dializami w Stacji Dializ DIAVERUM w Warszawie przy ul. Ceglowskiej 80, przy Szpitalu Bielańskim im. ks. J. Popiełuszki w Warszawie.

Wyniki. Podczas 174-miesięcznej obserwacji spośród 669 pacjentów (K-270, M-399) kwalifikowanych do powtarzanej dializoterapii, 84 (12,5%) miało nowotwór złośliwy pozostający w czasowej i/albo przyczynowej relacji z rozpoczynanym leczeniem. Możliwa była analiza losów 64 pacjentów dializowanych aż do końca obserwacji (5 zaprzestano leczenia hemodializami, u 5 częściowo powróciła czynność nerek, 10 zmieniło ośrodek dializ). Zmarło w czasie hemodializoterapii 57 z nich, u 1 wykonano przeszczepienie nerki, 6 kontynuuje hemodializoterapię (1-84 miesiące).

Wnioski. Leczenie nerkozastępcze powinno być rozpoczynane u pacjentów z nowotworami w sytuacji, kiedy pojawiają się do niego wskazania, tak jak w całej populacji osób z zaawansowaną chorobą nerek. Przeżywalność w tej grupie pacjentów jest względnie długa.

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INTRODUCTION

Despite the increased life span of the chronically dialysed patients, which parallels the total population, not many studies devoted to haemodialysed (HD) patients report the influence of neoplastic disease on their survival (1-5). That is probably because qualifying the neoplastic patients to the chronic RRT would still result in much opposition in many countries. In places where access to the RRT is limited, qualification to the RRT program is more demanding, and the treatment is offered to patients with better prognosis. To the contrary, where one would be easy to find a possibility to dialyse, the ethical aspects of such a therapy, the interference of medicine into the human life, the permissibility of futile therapy, etc. are taken into consideration.

These, and probably many other factors influence the objective fact – there are not so many studies devoted to the neoplastic patients in demand of RRT. Moreover, these studies usually focus on particular oncologic disorders, and those on multiple myeloma outnumber the other (6, 7). Do these patients, in the common feeling representing much worse prognosis as compared to others, really live for such a short time that they emerge only in the very little number of papers? In many studies performed in dialysed patients, an influence of such parameters as age, quality and type of dialysis access, or different biochemical factors (e.g. haemoglobin, albumin, parathormon, C-reactive protein) on mortality would be analysed, but the coexisting neoplastic diseases is mentioned only seldom, if at all (8). Would really so few neoplastic patients commence the RRT program, do these patients have such a short expected life expectancy, or this particular group is so difficult to study?

AIM

The aim of this study was to analyse the life span and outcomes of patients commencing RRT with coexisting malignant neoplasm, for whom commencement of the RRT had been strictly related (time and/or cause relation) with a neoplastic disease. The secondary aim was to analyse the causes of death in this population.

MATERIAL AND METHOD

The retrospective search of all medical records of patients commencing dialysis due to the acute or chronic renal failure through the 174 month between January 1, 2001 and June 30, 2015 at the Diaverum Dialysis Unit (former Non-Public Health Care Unit “Centre of Dialysis and Diagnostics”) at the Priest J. Popieluszko Bielański Hospital in Warsaw was performed.

RESULTS

In the years 2001-2015 (till June, 30) 669 adult patients (270 females and 399 men) initiated RRT with an intention to enter the chronic HD program. Out of these, 84 (12.5%) were diagnosed with neoplastic disease time- and/or cause-related with the beginning of RRT. For 14 patients (14/84, F-7, M-7) kidney dysfunction was acute (acute kidney inju-

ry – AKI). In 70 patients (70/84, F-18, M-52) the deterioration of kidney function was time-related to diagnosing the neoplasm. In the group of neoplastic patients commencing RRT (n = 84) the improvement of kidney function was observed in only 5 cases, all of them presenting with AKI (35.7% of AKI patients). Out of 79 patients demanding continuous haemodialysis therapy the outcomes of 64 patients on HD at the end of observation were analysed – 10 patients moved to other dialysis unit, 1 has been transferred to peritoneal dialysis, 4 stopped the RRT shortly after its initiation (in 1 case because of the lack of consent to continue, in 3 cases following the decision of the ethics committee with an intention to avoid persistent therapy). The observed outcomes were as follows: 57 of the 64 patients died on RRT program, 1 patient after the due time of deferment was successfully transplanted, 6 patients continued HD program lasting for 1-84 months, as of June 30, 2015 (fig. 1).

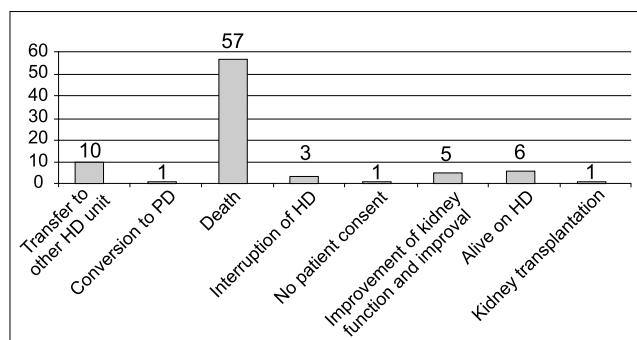


Fig. 1. Outcomes of 84 patients with active neoplastic disease commencing RRT in the years 2001-2015.

The deceased patients

Table 1 presents the characteristics of the population of deceased patients (n = 57), for whom HD was continued from the start of RRT despite the diagnosis of neoplastic disease. Indications to commence the RRT were classical. In case of AKI attempt to futile therapy was excluded, and in patients with chronic renal failure the general good condition, beside neoplastic disease, and predicted survival, were taken into consideration. Comparing the RRT and the conservative therapy's pros and cons and the individual patient's preferences were taken into account (including patients refusal and decision to interrupt therapy).

Most of the 57 continuously HD treated deceased patients, for whom RRT was initiated despite the coexist neoplastic disease and for whom start of the RRT was with independent time- and/or cause-related were of mean age of 69 ± 11.1 years. Males were a little bit older, and they also dominated the population in number. The largest group consisted of patients with haematological neoplasms – 16 persons (28.1%), including myeloma

multiplex – 13 persons (22.8%). Another big group were patients with cancers of the urinary tract (kidney cancers, cancers of the bladder) – together 14 persons (24.6%). Males with prostate cancer numbered 9 persons (15.8%).

Table 2 presents types of the neoplastic disease therapy in the deceased patients. It seems worth to notice that radical therapy was initiated in only 15 patients (23.3%, attempts of complete neoplasm resection) and most of patients received exclusively a palliative – 17 persons (29.8%), or symptomatic treatment – 19 persons (33.3%).

Table 1. Characteristics of the population 57 deceased patients, commencing RRT with consciousness of neoplastic disease and for whom start of the RRT was in an independent time- and/or cause-relation with neoplastic disease.

Population			
	n = 57	Females (n = 20)	Males (n = 37)
Age at the moment of initiation the RRT, mean	69.2	65.1	71.3
SD	11.1	10.3	11.0
min	48	48	52
max	88	82	88
Neoplasms			
Haematologic neoplasms	16	7	9
Myeloma multiplex	13	5	8
Kidney cancer	9	2	7
Cancer of the bladder	5	0	5
Prostatic cancer	9	–	9
Cancer of the uterus	6	6	–
Ovarian cancer	1	1	–
Mammal cancer	1	1	0
Lung cancer	2	0	2
Colorectal cancer	3	0	3
Cancer of the bile ducts	2	1	1
Cancers with non-established onset point	2	1	1
Melanoma malignant	1	1	0

Table 2. Therapeutical options used by oncologists in the 57 deceased patients, for whom the RRT was commenced despite the neoplastic disease.

Treatment			
	n = 57	Females (n = 20)	Males (n = 37)
Radical therapy	15	4	11
Palliative therapy	17	6	11
Symptomatic therapy	19	8	11
Non-consent for diagnostics or oncologic therapy	4	1	3
Observation – no therapy	2	1	1
Together: treated and non-treated	57	20	37

Despite all these patients ended up with the decease, it should be also clearly stated that majority of them reached relatively long survival time of 23 ± 40.4 months (F – 23.2 ± 28.4 , M – 26.5 ± 46.2 months). The longest demonstrated

survival, of 240 month – was observed in a patient after bilateral nephrectomy for cancer of both kidneys, who commenced dialysis therapy nearly 20 years ago, lived for 13 years with a functioning graft and next, has returned to dialysis for more 3 consecutive years.

Causes of the deceases of analysed 57 patients are presented in the table 3.

Table 3. Causes of decease in 57 patients, for whom RRT was commenced independent to time- and/or cause-related neoplastic disease.

Causes od deceases			
	Total	Females	Males
Neoplasms	39	14	25
Neoplasm most likely (decease off the hospital)	3	0	3
Subtotal – deceases of neoplasms	42	14	28
Infectious causes	6	2	4
Congestive heart failure	2	0	2
Myocardial infarction	1	1	0
Cardiac arrest (during implantation of the sequent HD catheter)	2	2	0
Cardiac arrest (during embolectomy of the femoral artery)	1	1	0
Cardiac arrest (after cerebral infarction)	1	0	1
Cardiac arrest (after bleeding from gastrointestinal tract)	1	0	1
Another (bowel necrosis)	1	0	1
Subtotal – deceases of non-neoplastic reasons	15	6	9
Total	57	20	37

In 39 patients, the advanced neoplastic disease caused the decease. In 3 other cases the decease occurred at home or in a hostel, and no medical death certificate could be obtained. Thus, on the ground of disease course the assumption was made, that the death resulted from neoplasm. It should be stressed out, that of 39 deceases caused by neoplastic disease only 5 were caused because of myeloma multiplex (12.8%), although the disease was diagnosed in 13 (22.8%) of the 57 deceased patients. For majority of patients presenting with others neoplasms, these neoplasms were the direct cause of death.

Infection was the second important cause of death (10.6%) – 5 cases patients developed sepsis (2 catheter-related, 1 after allotransplantation of the bone marrow, 1 as a complication of the bronchopneumonia with fulminant course, and 2 of non established etiology, probably originating within the urinary tract), and one died of fulminant bronchopneumonia. Only three patients died from cardiovascular reasons (5.3%). There were also sudden deceases directly related to non-cardiovascular causes – vascular manipulation (implantation of temporary HD access, at femoral artery embolectomy, haemorrhagic cerebral

infarction, severe bleeding from the upper gastrointestinal tract). Thus, to the contrary of the general HD population, cardiovascular complications constituted an infrequent cause of death in patients presenting neoplastic disease. One can assume, that the neoplasm kills these patients before the cardiovascular pathology does. How much earlier it happens remains to be established.

Patients with improved kidney function

Out of the 84 patients included to the RRT during the analysed period and presenting with neoplastic disease AKI was diagnosed in 14 (16.7%). In 5 of these patients, the kidney function improved and in the HD could have been discontinued. This group was composed of 3 females with myeloma multiplex on palliative treatment, one male with prostatic cancer and tubulo-interstitial nephritis and one male with acute pre-renal kidney failure and lung cancer. Thus, our analysis revealed the 35.7% recovery rate from neoplasm-related AKI (5 out of 14 cases).

Patients alive and on HD

In 6 patients (6 males, 0 females) included to the RRT during analysed time, haemodialysis therapy continues. Table 4 presents the diagnosis and time on RRT as of the end of observation. In this group the longest survival time reached a man, presenting at the RRT commencement in the age of 63 years, with the prostate and kidney cancers.

Table 4. Patients still continuing HD, for whom RRT was commencing RRT with consciousness of neoplastic disease and for whom start of the RRT was in an independent time- and/or cause-related with neoplastic disease.

No.	Age at the moment of initiation the RRT	Diagnosis	Time on RRT in months (and still growing)
1	65	Prostate cancer	1
2	59	Kidney cancer	13
3	74	Myeloma multiplex	22
4	86	Prostate cancer	36
5	61	Prostate cancer	57
6	63	Prostate cancer and kidney cancer	84

DISCUSSION

The increasing, year-by-year, prevalence of patients on chronic RRT in the elderly, for whom the neoplastic disease has been not diagnosed till the qualification to the dialysis program, discerned also at our unit, undoubtedly triggered this retrospective analysis. The diagnosis of cancer made just prior to the planned or urgent start of RRT calls for additional difficult evaluation of patient's prognosis, including the one on potential eligibility to kidney transplantation. Sometimes this evaluation has to be intuitive – the urgent decision

is to be taken during the hospital duty, under the pressure of rapid clinical or biochemical indications, and with no possibility of calling the ethics committee meeting prior to the catheter placement. Although in cases of AKI the “Yes” decision comes relatively easy, one have to consider that, especially in the elderly, AKI is frequently superimposed on the CRF, which makes the future cessation of treatment not possible. This happened in 64.3% of our AKI patients presenting with neoplasm. The other problem creates the uncertainty if the patient's disorientation considered transient and secondary to uremic condition, is not in fact permanent and resulting from chronic dysfunction and lesion of the central nervous system. Population initiating RRT is becoming older and older, and thanks to progress in medicine, patients are ready to live longer and longer. Thus, they reach the moment in their live when neoplastic disease presents accompanied by atherosclerotic changes which decrease the glomerular filtration rate – simultaneous and cause-related. The “No” decision is not so easy, as well. Literature data describing patients with acute kidney injury coexisting with neoplastic disease may be understood as an effect of increasing year by year acceptance to the RRT for these patients (9, 10). Even so, only singular publications are devoted to the CRF patients on dialysis. Much more easy are to be found studies applicable to neoplasms incidence (especially in the urinary tract) in population with renal failure (11-14). Results presented here indicate, that in patients with diagnosed neoplasm only in 4 cases out of 84 RRT had been discontinued, which was determined by the intention to avoid persistent therapy in 3 cases and to considerate conscious patients will in the last one. For 4 patients out of 57 deceased during RRT – this treatment with haemodialysis was continued despite no patient consent for diagnostics qualified to the oncological therapy (male with prostatic cancer) or for chemotherapy (3 patients with multiple myeloma).

Interesting conclusions are outcome from analyse survival time and causes of deceases in patients dialysed with neoplastic disease coexisting at the moment of start RRT. In Verdalles et al. study describing outcomes of 139 patients over 75 years of age and commencing RRT – mean survival time was 3.3 ± 2.2 years, neoplasms were a cause of death in 23.7 (15). Our patients with neoplasms were a little bit younger – they were meanly over 69 years. Even so, the survival time patients undergoing haemodialysis was shorter, of mean over 2 years, but still relatively long.

The majority of our patients deceased because of neoplasm. Infectious causes, especially sepsis caused by infection of the vascular access, are still a sad reality, which took 6 of our patients. Our patients died seldom from cardiovascular reasons, contrary to what is observed in the RRT patients with no neoplastic disease at the RRT initiation. Acute cardiac deceases in our material were linked to specific procedures or clinical situations – vascular manipulation (implantation of

the catheter, embolectomy) or bleeding (bleeding from upper part of gastrointestinal tract, cerebral infarction secondary haemorrhagic). Cardiovascular deceases were only 15.8% (9/57), it mean they were 3.5 times less frequent than in general dialysed population (16).

Powerful side of our elaboration is fact of analyse data from more than 15-year observation of wide group dialysed patients, in whom even 12.5% (84/669) were patients commencing dialysis therapy with active neoplastic disease at the moment of start. However undoubtedly such investigation – retrospective, observational and one-unit – is unable to exhaustively characterize all population and is burdened with all imperfections of this retrospective method. Contrary to this, with satisfaction we might underline fact, that process of qualification done in our unit, is not discriminating any neoplastic patients, giving chance to them to evidently prolong their lives.

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.

CONCLUSIONS

Renal replacement therapy (RRT) should be initiated in patients presenting with neoplastic disease whenever the indications to that treatment exist, just alike all the CRF population. In these patients the life expectancy on RRT can be quite long. The RRT for acute renal injury (AKI) can be withdrawn only in every third patient presenting neoplastic disease, but the remaining two in three will continue, even for years on the chronic RRT program. The decision to commence or to terminate the RRT in patients presenting neoplastic diseases for both the acute and the chronic RRT, as well as the choice of RRT modality, must result from the all-embracing team-analysis of the pros and cons of such a therapy.

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