

The outcomes of limb-sparing surgery of patients with chondrosarcoma of the pelvis

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Introduction. Chondrosarcoma (ChSa) is the second most common primary malignant bone tumour, after osteosarcoma. The aim of this study is to analyse the prognostic factors in patients operated on ChSa of the pelvic bone with limb sparing on the basis of a large retrospective group of patients. Aspects of the surgical technique are also presented, taking into account the location of the tumour within the pelvis. An attempt was also made to define the criteria for selecting patients for whom radical and limb-sparing surgery is possible.

Material and methods. We analysed 53 consecutive patients with chondrosarcoma of the pelvic and sacral bones after surgery performed at the Department of Soft Tissue/Bone Sarcoma and Melanoma in Maria Skłodowska-Curie National Research Institute of Oncology in Warsaw, Poland, between 1998 and 2020. Patients had surgery with sparing of the lower limb with the intention of cure.

Results. There were 34 patients with G1 grade, G2 – 16, and G3 – 3. The R0 resection margin was achieved in 36 cases, the R1 margin in 11, and the R2 margin in 5 cases. The 5- and 10-year overall survival rates for the entire group were 84% and 65%, respectively. The 5-year and 10-year disease-free survival (DFS) probabilities were 65% and 43%, respectively.

Conclusions. Multivariate analysis of the studied group of patients showed that the resection margin was a statistically significant factor determining prognosis (patients after R0 surgery margin have about 5 times lower death risk compared to patients after non-radical surgery with R1 or R2 margin).

Key words: chondrosarcoma, pelvic bone, resection margin, histological malignancy grade

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Introduction

Chondrosarcoma (ChSa) is the second most common primary malignant bone tumour, after osteosarcoma [1]. The majority of cases are diagnosed in patients above 50 years of age. Most frequently this cancer develops in flat bones or in limb girdles and proximal parts of long bones [2–6]. Men are more often affected.

The most frequently observed chromosomal anomalies in ChSa are: 9p21, 17p13, 13q14,10. MYC gene amplification and the amplification of the gene coding the AP-1 protein also plays an important role in the ChSa pathogenesis [5, 7].

ChSa can be divided into conventional types (approx. 85–90%) and non-conventional. Conventional (classic) ChSa is a cancer which is resistant to chemotherapy and radiotherapy. The only effective treatment methods remain surgical intervention with a radical margin [5–10]. Non-conventional forms of ChSa such as: clear-cell chondrosarcoma (1–2% of all chondrosarcoma cases), de-differentiated chondrosarcoma and mesenchymal chondrosarcoma, which make up about 10% of all chondrosarcoma cases, respond, in some degree to systemic treatment, or, possibly to radiotherapy [1, 11].

This work concerns all patients with ChSa with the exception of the mesenchymal type (on account of a different method of treatment of small-cell sarcomas). In ChSa, 3 histological grades can be distinguished (G1, G2, G3).

The majority of ChSa occurs spontaneously, yet 5% of ChSa are the outcome of the transformation of histologically mild tumours such as osteochondroma or enchondroma. That is why ChSa may be divided into primary and secondary types [1–4].

The most frequent symptom reported by patients and for which they seek medical advice for ChSa located in the pelvic bones is pain in the iliac and/or sacral area, often accompanied with the oedema of soft tissues. Apart from this – there is pain or difficulty when walking. These symptoms may persist for months or even years. Thus, they are frequently ignored by patients and even by doctors themselves. When the patient does finally get to an oncological centre, the disease is often locally advanced [12]. Sometimes a symptom may be an extensive and painless tumour or a lesion is found incidentally. Diagnosis is made on the basis of a biopsy collected from a tumour specimen. The biopsy should be preceded by imaging diagnostics (X-ray, CT and contrast enhanced MRI) [11].

The objective of this study is to analyse the prognostic factors in patients operated on for ChSa of the pelvic bone with limb sparing on the basis of a large retrospective group of patients from a reference centre for treatment of adult patients with sarcomas. Also, some aspects of the surgical technique are presented, taking into account the location of the tumour within the pelvis. An attempt was also made to define the criteria for selecting patients for whom radical and limb-sparing surgery is possible.

Material and methods

The analysis concerned 53 consecutive patients with chondrosarcoma of the pelvic and sacral bones after surgery performed

at the Department of Soft Tissue/Bone Sarcoma and Melanoma in the Maria Skłodowska-Curie National Research Institute of Oncology in Warsaw, Poland, treated between 1998 and 2020. These patients had lower limb sparing surgeries, the scope of which included the resection of specific fragments of pelvic bones, or sacral bone, sparing the function of the lower limb. These interventions comprised the resection of the entire iliac ala or its fragment, resections of the ischium and pubis, in one block or their fragments, resections of the hip joint with reconstruction with an endoprosthesis as well the resection of a fragment of the sacral bone, preserving the sacroiliac joint.

The prognostic value of the following factor was studied:

- age,
- sex,
- the largest dimension of the tumour (in centimetres),
- histological grade.

The histological grade was obtained on the basis of the protocols of histopathological assessment performed at the Pathomorphology Department of the Maria Skłodowska-Curie National Research Institute of Oncology. Moreover, the effect of the radicality of the intervention on the survival (R factor) was studied. The radicality of surgery was assessed on the basis of the protocols of histopathological assessment and surgery descriptions. The R0 resection meant that in the histopathological assessment the surgical margins were free from the presence of tumour cells; during the surgery, the tumour pseudo-capsule remained intact. The R1 resection described the situations in which, during the surgery no macroscopic tumour presence was found on the resected sections, the tumour pseudo-capsule remained intact, whilst in the microscopic evaluation, the resection margin was not radical. The R2 resection comprised situations in which, during the surgery, the tumour pseudo-capsule was damaged, some part of the tumour was intentionally not resected on account of the lack of technical possibilities of a macroscopically radical resection; the macroscopic assessment revealed damage of the tumour pseudo-capsule, and the margin was not radical, both macroscopically and microscopically.

In 50 patients, the classic form of ChSa was diagnosed (with a distinction into histological grades: G1, G2, G3), and in 2 patients dedifferentiated ChSa was found, whilst in 1 patient, clear cell ChSa was diagnosed. ChSa patients with the mesenchymal form of the cancer and patients with the extraosseous form of ChSa were not included in the study. In 9 patients, a secondary form of ChSa evolving from osteochondromas was diagnosed. 46 out of the 53 patients operated on for the primary tumour were solely surgically treated till the moment of disease progression or the last follow-up (and 1 patient from this group was operated on in another centre); whereas out of the remaining patients, 3 received post-operative radiotherapy, and 3 – intraoperative brachytherapy and post-operative radiotherapy. One patient received pre-operative chemotherapy (the patient in whose case de-differentiated

chondrosarcoma was diagnosed from the material harvested in a surgical biopsy, and the final post-operative diagnosis was classic chondrosarcoma G3). In none of the patients qualified to surgical treatment of the primary tumour, were remote metastases found (M0).

The factors evaluating treatment efficiency were defined as the probability of overall survival (OS) and disease-free survival (DFS). The overall survival (OS) was measured from the date of the surgery till the date of death or the last information regarding whether the patient was alive. The disease-free survival (DFS) was measured from the surgery date till the date of disease progression, the date of patient death for any causes or the date of the last follow-up.

The prognostic value of factors such as: age, sex and the largest dimension of the tumour measured in centimetres, histological grade (G), and radicality of the surgery was assessed on the basis of statistical analysis.

The univariate analysis was performed with the use of the log-rank test on the level of statistical significance of 0.1 [12].

The multivariate analysis was performed with the use of the Cox proportional hazard model [13]. In the modelling process, the stepwise selection of variables was used, adopting the standard exclusion thresholds: $p > 0.1$ and inclusion thresholds $p < 0.05$. The analysis was made with the use of the IBM SPSS Statistics 23.0 package.

Results

Patients' characteristics

The studied group of patients comprised 24 women and 29 men. Their age ranged between 17 and 71 years with the median age being 42 years. There were 34 patients with G1 grade, 16 with G2 and 3 with G3. The tumour size measured in centimetres varied between 3 and 37 cm (median 10 cm). The R0 resection margin was obtained in 36 cases, the R1 – in 11, and the R2 – in 5. The characteristics of the analysed group is presented in table I.

Resection types of pelvic fragments with limb sparing

Aspects of surgical technique

In the analysed group of 53 patients, the following types of resections were made: the resections of the fragment of or an entire iliac ala in 25 patients, the resections of the ischium and pubis or only pubis in 17 patients and the resections of the hip joint with a reconstruction with an endoprosthesis – 6 patients; the resections of the sacral bone with sparing the sacroiliac joint or the resection of the areas of one of the sacroiliac joints – 5 patients (fig. 1).

The patient position for surgery was either a gynaecological one or lying in a contralateral side. Laying a patient on their side gives free access to the pelvis, both from inside and outside. Apart from this, it allows for control of the iliac joint

Table I. The characteristics of the analysed variables

Sex	
females	24 (45.3%)
males	29 (54.7%)
Age	
min.–maks.	17–71
median (IQR*)	42 (32–53)
G – histological grade	
G1	34 (64.2%)
G2	16 (30.2%)
G3	3 (5.6%)
R – resection margin	
**BD	1 (1.9%)
R0	36 (67.9%)
R1	11 (20.8%)
R2	5 (9.4%)
Tumour size (cm)	
min.–maks.	3–37
median (IQR*)	10 (8–11)

*IQR – interquartile range, n = 53; ** – no data

and for defining the appropriate level of resection. Moreover, it allows for better peritoneum control, so that the peritoneal cavity, if possible, is not open during surgery, which prevents the implantation of the tumour into the peritoneal cavity.

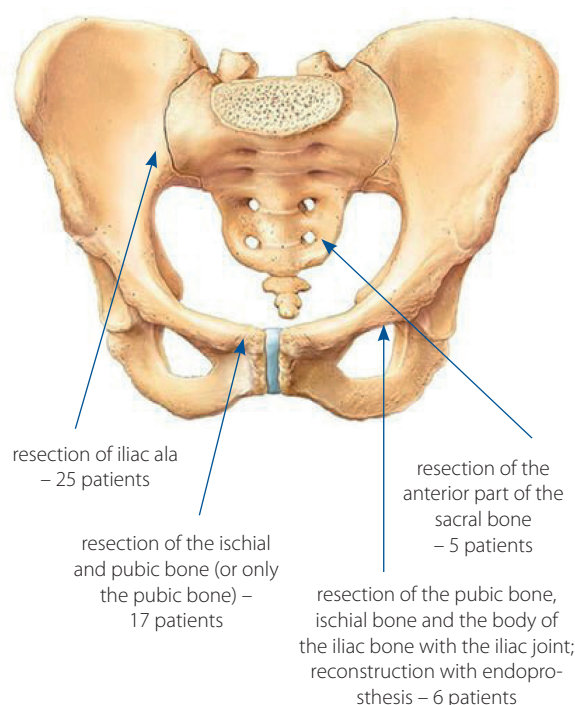


Figure 1. Resection scopes in the surgeries of pelvic bones sarcoma with limb sparing

What is more, when the patient is laid on their side, the peritoneal cavity may be moved onto the contralateral side. Patients operated on for a tumour located in the sacral bone had surgery while lying on their abdomen.

Analysis of patients' survival and the factors affecting the prognoses

As a result of the analysis, it was found that the 5- and 10-year overall survival for the entire group (with 95% confidence intervals [CI]) were respectively: 84% (72–95%) and 65% (47–83%). The follow-up scope, in months was: 0.689–356; median follow-up 90 (95% CI: 57–124). The OS curve is presented in figure 2.

The probability of disease free survival periods of 5 and 10 (with 95% CI) years were 65% (50–80%) and 43% (23–63%) respectively. The DFS curve is presented in figure 3.

In the univariate analysis which was performed, two factors with a statistically significant effect on OS and DFS ($p < 0.1$) were found: the histopathological grade (factor G) and resection radicalism (factor R). A statistically significant effect on OS was the G1 histopathological grade ($p = 0.011$) and R0 resection scope ($p = 0.007$). The same factors (G1 and R0) were found to affect the DFS: p values: 0.076 and 0.051 respectively. The results of the univariate analysis are presented in figures from 4 to 7.

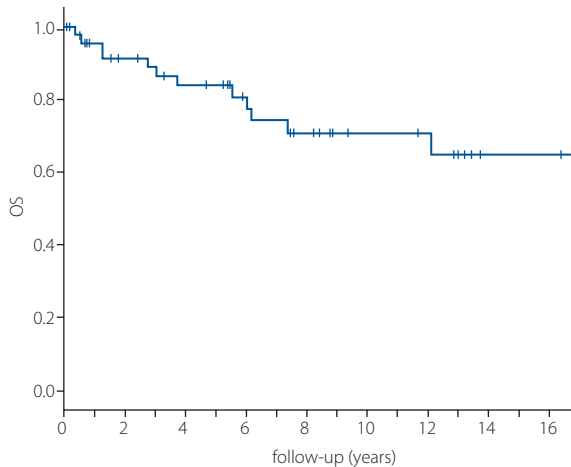


Figure 2. Overall survival (OS) for the entire group

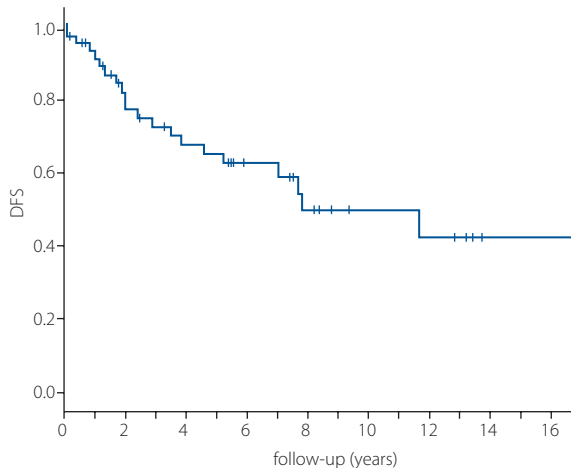


Figure 3. Disease-free survival (DFS) for the entire group

The Cox multivariate analysis allowed one to observe that only the radicality (R0 resection) of the surgery affects the overall survival and progression free survival. The relative risk of death in patients with an R0 resection makes up 0.206 of the respective risk for patients with R1 and R2 resections (i.e. patients with an R0 resection have approx. 5 times lower risk of death than patients with R1 and R2 resection). The risk of disease progression with resection R0 makes up 0.371 of the respective risk for patients with resection R1 and R2 (i.e. patients with an R0 resection have approx. 3 times lower risk of disease progression in comparison with patients with resection R1 and R2). The results of the multivariate analysis are presented in table II.

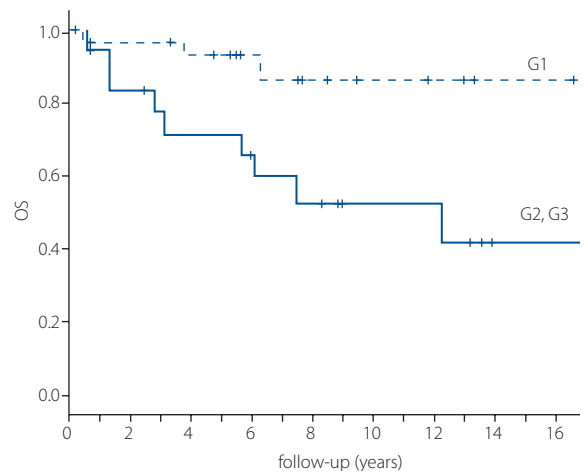


Figure 4. Overall survival (OS) depending on histological grade G. G1 – low histological grade; G2 – medium histological grade; G3 – high histological grade. Probability of 5- and 1-year survival (OS) depending on histological grade were 94.6% and 85.6% for the G1 patients, and: 71.6% and 52.3% for the G2 and G3 patients, respectively

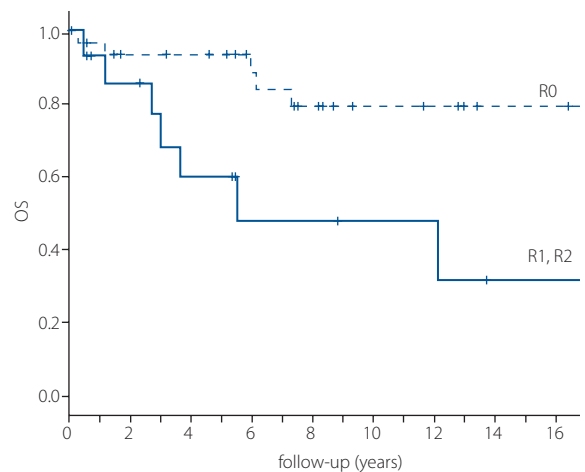


Figure 5. Overall survival (OS) depending on the radicality (R) of the surgery. R0 – radical resection, margin microscopically free from the cancer cells; R1 – microscopically non-radical resection; R2 – macroscopically non-radical resection. Probability of 5- and 10-year overall survival (OS) depending on the resection margin were: for the patients with R0 margin: 76% and 60%, whilst for the patients with R1 and R2: 40% and 20% respectively

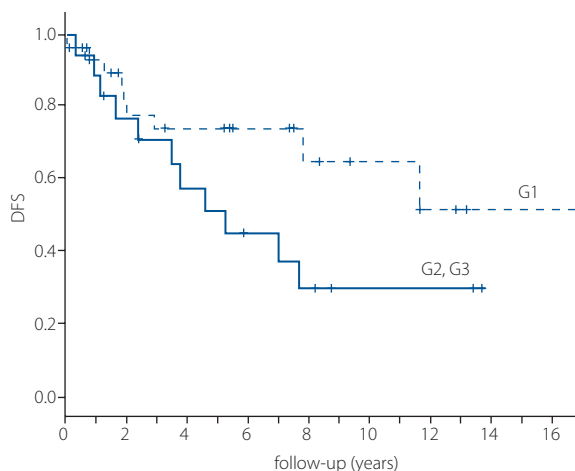


Figure 6. Disease-free survival (DFS) depending on histological grade G. G1 – low histological grade; G2 – medium histological grade; G3 – high histological grade. Probability of 5- and 1-year disease-free survival (DFS) 5 depending on histological grade were for the G1 patients: 75.7% and 65%, and for the G2 and G3 patients: 52.9% and 31.2% respectively

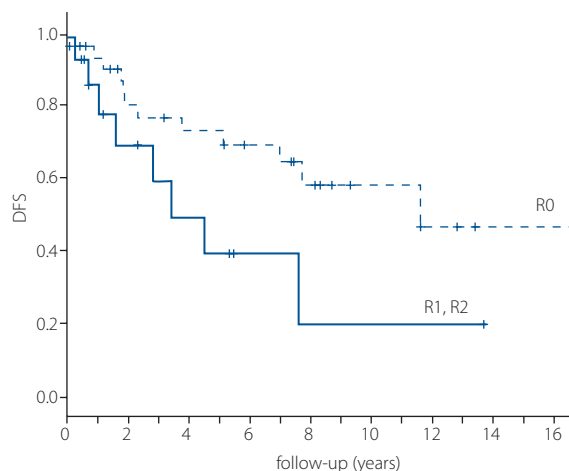


Figure 7. Disease-free survival (DFS) depending on the radicality (R) of the surgery. R0 – radical resection, margin microscopically free from the cancer cells; R1 – microscopically non-radical resection; R2 – macroscopically non-radical resection. Probability of 5- and 10-year disease-free survival (DFS) depending on the resection margin were: for the patients with R0 margin: 75.2% and 60%; whilst for the patients with R1 and R2: 20% and 40% respectively

Table II. The results of multivariate analysis – the final regression model parameters in Cox proportional hazard model

Dependent variable	Independent variable	Beta factor	Statistical error	Wald's test	p	Relative risk	95% CI – threshold:	
							upper	lower
risk of death	male sex	1.111	0.675	2.711	0.100	3.037	0.809	11.397
OS	R0	-1.578	0.604	6.825	0.009	0.206	0.063	0.674
risk of recurrence	male sex	0.783	0.478	2.685	0.101	2.189	0.858	5.588
DFS	R0	-0.992	0.475	4.355	0.037	0.371	0.146	0.941

Complications

None of the patients died within the period of 30 and 90 days from the date of surgery. In 53 operated patients, the following complications were observed:

- 1 patient was operated on for the urinary bladder fistula (15 days from the surgery),
- 1 patient was operated on for an abscess in the post-surgical wound (10 days from the surgery),
- 4 patients were operated on for post-operative wound bleeding or a haematoma (within the range between 0–26 days from the surgery),
- 1 patient was operated on for luxation of the iliac joint prosthesis (3 days from surgery).

In total, complications requiring surgical interventions were found in 7 patients (13%).

Such situations as the necessity of puncture on account of lymph accumulation in the surgical wound or a poor limb function were not taken into consideration. Lymph drainage from the surgical wound and the necessity of rehabilitation are the results of surgery and are included in the post-surgical protocol.

Discussion

As a result of the statistical analysis, it was observed that the core factor affecting the overall survival (OS) and disease free survival (DFS) of patients with ChSa localised in the pelvis is the resection margin. Patients with an R0 resection have a higher probability of survival and disease free survival than those patients where a R1 or R2 resection have been performed, irrespective of tumour size or histological grade.

J. From, A. Klein, Baur-Melnyk A. et al. [14] carried out an analysis of 87 patients observing that a radical resection margin (R0) significantly affects disease free survival, whilst it does not have any effect on overall survival. It must be observed however, that the survival period was analysed in patients with various locations of ChSa (upper or lower limb, trunk and pelvis). The analysis revealed that once location is taken into consideration, the patients with ChSa located in the pelvis had the worst prognoses. In the entire group, in turn, the factor which affects survival the most is the histological grade (and also the presence of metastases) [14]. In the analysed group of 53 patients with pelvic ChSa, only

the univariate analysis revealed that the histological grade affects the OS and DFS.

Another research [15] performed by X. Chen, L.J. Yu, H.M. Peng et. al presented an analysis as to whether the resection margin (R1 vs. R0) in patients with ChSa G1 affects overall survival or disease free survival. The multi-centre analysis showed that with the G1 grade, a non-radical margin does not affect the probability of recurrence. It must be remembered that this was a multi-centre analysis, which took into consideration mostly limb locations of ChSa, so the study group was not homogenous. It seems that in the case of the pelvic location of ChSa, irrespective of the histological grade, surgical intervention should be planned in such a way that a microscopically radical margin should be obtained.

Other authors – Y. Tsuda, S. Evans, J.D. Stevenson et al. [16] – declare that a resection margin of at least 1 mm guarantees progression free survival. Yet their study solely concerned patients with secondary ChSa which had evolved from a osteochondroma. It was also a multicentre analysis.

The analysed group of 53 patients was comprised of patients treated in one centre (with the exception of 1 patient operated on for a primary tumour outside the institute); also 1 location (pelvis) was taken into consideration; moreover about 70% of patients were operated on by surgeons as the main operators.

Therefore, this can be regarded as quite a uniform patient group with respect to the conditions in which they were treated.

It must be added that in this work there was no division of margins into smaller 1 mm and at least 1 mm (the R0 margin was defined as a margin free from tumour cells – the smallest one is the tumour capsule on condition that it remained intact during the procedure).

As the analysed group of patients (53 patients after resection of the pelvic bone, and sparing the limb) is homogenous (so the effect of the same factors on patients within the process of treatment can be assessed), the conclusion that the result of the multivariate analysis shows that the best prognoses concern the patients with R0 resection is very probable.

Similar conclusions were reached by the team of C. Zoccali, J. Baldi, D. Attala et al. [5], who showed in their study that the R0 margin in surgical treatment of patients with pelvic ChSa is the most significant factor which determines the prognosis, in contrast to patients with ChSa of long bones, where the R1 margin in patients with ACT, i.e. ChSa G1 is not a significant prognostic factor. Similar conclusions were also drawn by the authors of other studies [8, 9]. Our analysis confirms these results. Examples of diagnostic images of patients operated on for chondrosarcoma of the pelvis, before and after surgery, are presented in figures from 8 to 10.



Figure 8. Female patient, aged: 69; iliac joint resection with endoprosthesis – pre-op (A) and post-op (B)

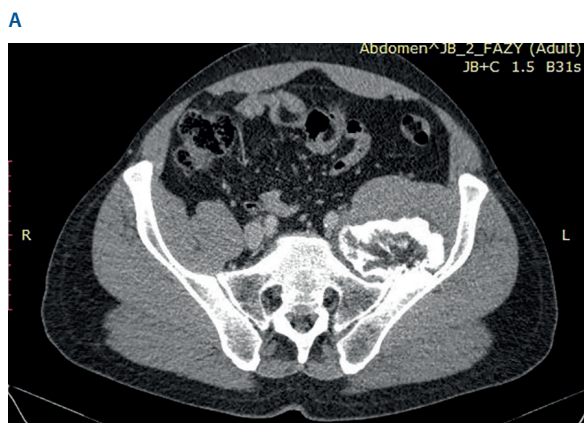


Figure 9. Male patient, aged: 41; chondrosarcoma of the iliac ala and left sacroiliac joint – CT image pre-op (A) and post-op (B)

A



B

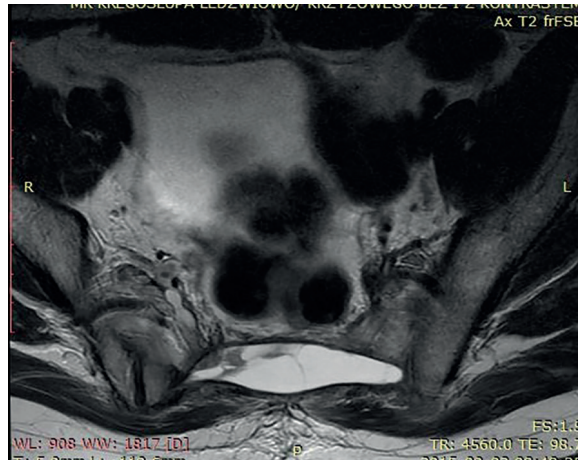


Figure 10. Male patient, aged: 39; chondrosarcoma of the sacral bone – MRI image pre-op (A) and post-op (B)

Conclusions

The univariate analysis performed in a group of 53 patients operated for chondrosarcoma of the pelvis, with limb sparing, allowed to name the following factors affecting the overall survival (OS) and disease free survival (DFS): tumour histological grade (G) and resection margin (R). The best prognoses are associated with G1 grade and R0 resection margin.

The multivariate analysis showed that the factor which affected overall survival (OS) and disease free survival (DFS) was resection margin (R). The best prognoses are associated with R0. The success of treatment with the radical margin depends on appropriate qualification – first of all on the basis of imaging diagnostics – and surgical technique (worked out on the basis of many years' experience).

It can be concluded that the treatment success depends on the length of experience of a given centre which performs such interventions, i.e. resections of the fragments of the pelvic bone sparing the limb with an intention to achieve a radical margin (R0).

Conflict of interest: none declared

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